American Journal of Obstetrics and Gynecology

VOL. 32 NOVEMBER, 1936 No. 5

Original Communications

THE RÔLE OF THE LOWER UTERINE SOFT PARTS IN LABOR*

WILLIAM E. CALDWELL, M.D., HOWARD C. MOLOY, M.D., AND ANTHONY D'ESOPO, M.D., NEW YORK, N. Y.

(From the Sloane Hospital for Women.)

INTRODUCTION

DURING the last three years at the Sloane Hospital for Women and the Roentgen Ray Department of Presbyterian Hospital, we have made extensive use of the roentgen ray in the study of fetal-pelvic relationships during labor. We have accumulated a comparatively large series of roentgenologic case studies, which, in many instances, consist of two or more sets of stereoroentgenograms for each patient, obtained at intervals during the first and second stages of labor. The method of delivery in the patients studied has varied from cesarean section after a trial of labor to a normal spontaneous delivery, so that we have had the opportunity of studying changing fetal-pelvic relationships in abnormal as well as in normal parturition.

The opportunity of comparing the fetal-pelvic relationship early in labor with the position which exists later, near the beginning of the second stage, has shown us the variable manner in which the fetal head may descend in relation to the pelvic cavity. Our observations have led us to attribute considerable significance to the lower uterine segment and its fascial attachments to the pelvic walls as the expla-

*Read at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25 to 27, 1936.

nation of these variations in the position of the pelvic axis of fetal descent. In the present report we wish to describe extreme examples of these variations, to explain the manner in which we believe the lower uterine segment and its supporting structures cause these diverse fetal-pelvic relationships, and, finally, to make brief reference to the resultant effect on the mechanism of labor in relation to the type of pelvis and the clinical course of labor.

METHODS

A complete roentgenologic examination during labor should include anteroposterior stereoroentgenograms obtained in the supine position and a large lateral film. The stereoroentgenograms and the lateral film should be compared to note any changes in the relationship of the fetal axis to the inlet or in the position of the head with respect to the pelvis which may occur unless the head is fixed in the pelvis. These differences between fetal pelvic relationships may be described as follows:

1. The anteroposterior roentgenogram may show that the fetal axis is markedly posterior to a perpendicular line from the inlet, while, in the same case, the lateral view may show that, as the uterus sags forward, the fetal axis becomes more perpendicular to the plane of the inlet.

2. The lateral film may also show that the fetal body and head have rotated slightly from the position which existed when the stereoroentgenograms were obtained.

3. Unless the head is fixed in the lower uterine segment it may be dislodged to a higher level in the pelvis when the lateral position is assumed. Or, in a few cases, it may actually descend to a lower level than the stereoscopic view revealed by virtue of the fact that the fetal body becomes more perpendicular to the inlet.

Anteroposterior stereoroentgenograms show undistorted spacial relations of head to pelvis and, for that reason, are superior to lateral views in the study of those variations in the fetal axis of descent which represent the chief objective of this present investigation. There are a number of reasons why the lateral views are not as satisfactory for this purpose. In the first place it is difficult to place the patient so that the anteroposterior diameter is parallel with the film. It is equally difficult to center the central ray at right angles to the anteroposterior diameter. Finally, the enlarged shadow image of the fetal head within the pelvic cavity, as seen in the lateral film, makes it difficult to appreciate its axis of descent in relation to the symphysis in front or the sacrum behind.

During labor the wet stereoroentgenograms may be viewed in the ordinary stereoscope and for practical purposes a true concept of the

spacial relationship of head to pelvis can be obtained. However, it is impossible to accurately control the size of the stereoscopic image of head and pelvis and we believe that some attempt to correct this undesirable physical fact is helpful. We have perfected a practical model of the precision stereoscope to serve this purpose. The wet films can be viewed immediately but, since the presence of developing frames makes it difficult to place the film correctly over the view box, some distortion of the image is inevitable, even in the precision stereoscope, though present to a lesser degree than would occur with the ordinary stereoscope. In a few cases the films, even when dried and viewed correctly in the precision stereoscope, may not be suitable for measurement, because the patient, through the discomfort of active labor, may move during the interval between the stereoscopic shift. However, under both circumstances, the precision stereoscope reconstructs a more accurate image with less distortion than occurs with the ordinary flexible stereoscope. These objections to the use of the ordinary stereoscope, for viewing either the wet or dried films, are not serious enough, however, to preclude its use when the observer is aware of the principles of stereoscopic distortion. The precision stereoscope makes it possible to see an exact reproduction of the pelvis and the fetal-pelvic adaptation. Any measurement desired may be taken. We are convinced that viewing the actual pelvis and seeing the fetal-pelvic adaptation are much more important than any linear or volumetric measurements.

OBSERVATIONS

(A) Normal Mechanism of the Lower Uterine Segment

In a recent publication[1] we discussed the general pattern of normal labor and made reference to the rôle of the lower uterine segment in molding and directing the head downward and backward into the pelvic cavity during engagement and descent. In view of the fact that at this time we concerned ourselves largely with variations in the position and degree of this downward and backward curved axis of descent, we must first briefly review the principles involved in the normal mechanism.

In normal labor the axis of the lower uterine segment causes the head normally to follow an axis in the posterior segment of the pelvis in relation to the sacral curve. This control exerted by the lower uterine segment and its supporting structures may be termed its "guiding" or "directing" influence. At the same time it causes flexion and molding of the fetal head. The degree of flexion or molding is, to a certain extent, dependent on whether the membranes are intact or ruptured.

Before the time of Robert Barnes[2] the function of the lower uterine soft parts was imperfectly understood. In 1869 he described the curved axis of descent referred to and attributed considerable significance to the inclined plane of the anterior wall of the lower uterine segment, believing that this plane deviated the head downward and backward into the hollow of the sacrum. He termed it the anterior or first "uterine valve." Barnes' views have received but scant recognition by modern obstetric authorities. We believe our observations have confirmed Barnes' principles, but the use of the roentgen ray has enabled us to study the effect which the factors outside of the lower uterine segment, especially the character of its fascial supports, may exert in modifying the position and degree of this curved axis of descent.

Further study of many x-ray examinations of normal and abnormal labor has convinced us that apparently the axis of the lower uterine segment does not always correspond to the optimum axis of the pelvic canal. In analyzing these cases we have arrived at the conclusion that the axis of the lower uterine segment must be influenced by its fascial attachments to the bony pelvis and that variations in this axis, caused by such attachments, exert a profound influence on the mechanism of labor.

The guiding influence of the lower uterine segment in normal labor and the principle of the variations in its axis, which concern us especially at this time, are illustrated in the case study shown in Fig. 1. The lower uterine segment has been outlined by the use of 6 per cent sterile sodium iodide solution held under pressure in the vagina at the time the roentgenograms were obtained. In the first roentgenogram obtained early in labor the head was situated over the fore-pelvis close to the symphysis, L. O. T. position, posterior parietal presenting and dipping well in the inlet. The sodium iodide was injected when the cervix was approximately three fingers dilated and well thinned out. This method of visualizing the lower uterine segment was used in a few cases without harm to the patient.

The axis of the outlined lower uterine segment in Fig. 1 (long curved arrow), through which the fetal head is descending, is slightly downward and backward and, as near as can be determined, represents the degree of curvature which occurs in normal labor. The fascial supports, which modify the degree and position of this axis, are situated between the vagina and the rounded portion of the lower uterine segment in the position indicated "*X*," Fig. 1. Note that the length of "*A*," which represents the distance between the posterior aspects of the symphysis and the anterior portion of the dilating uterocervical junction, is greater than "*B*," the distance between the sacrum and the posterior aspect of the uterocervical junction. Variations in

the length, strength, or character of these structures, "*A*" and "*B*," Fig. 1, will naturally affect the position of the axis of the lower uterine segment, thereby guiding the head downward in one extreme close to the sacrum, or in the other close to the symphysis.

It will be noted that these variations in the position of the axis of the lower uterine segment are attributed to the length, strength, and character of the fascial attachments, situated at a low level just above the cervix, "*X*," Fig. 1. At a higher level, as indicated in Fig. 1, "*C*," the lower uterine segment is permitted a degree of movement independent of these lower fascial attachments, thereby allowing it to move in conjunction with the body of the uterus and the fetus to adjust its long axis to the uterine cavity. In the case of an abnormal pelvis, the lower uterine segment at higher levels, not being fixed, can

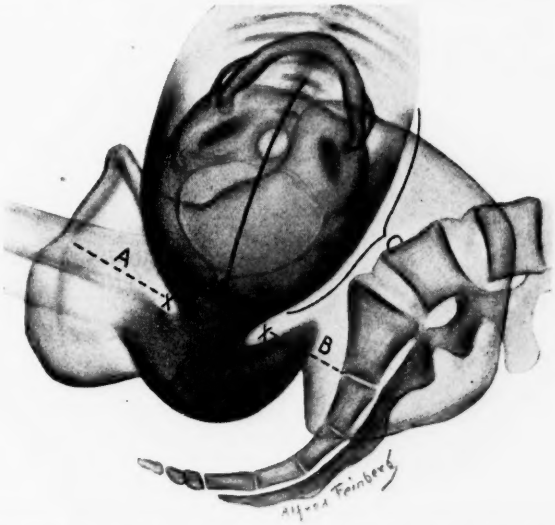

Fig. 1.—The lower uterine segment is outlined by 6 per cent sodium iodide which has infiltrated upward between the membranes and the lower wall of the uterus. Note the slight downward and backward axis of descent. Variations in the position of the axis of the lower uterine segment will result from differences in the lengths (*A* and *B*), strength, or character of the fascial supports originating from the utero-cervical junction at "*X*." The upper portion of the lower uterine segment "*C*" is freely adaptable to any particular fetal or uterine axis, and is flexible enough to allow fetal-pelvic adaptation to pelvic type at the inlet.

allow for any necessary adaptation from the standpoint of position in relation to the pelvis or asynclitism in relation to fetal piston axis. Thus, because of the freedom in movement possessed by the upper portion of the lower uterine segment, the fetus may be directed toward the inlet at practically any angle as a result of variations in the inclination of the pelvic inlet, variations in fetal piston axis, an inlet of abnormal shape, or the presence of relative disproportion.

Heretofore, obstetricians have placed considerable importance on these factors which modify the uterine axis in relation to the inlet.

Every conceivable method for measuring not only the bony pelvis itself, but also the inclination of the inlet as well, has been suggested without, however, supplying the full explanation of all the difficulties met. It is true that in certain individual cases labor may be prolonged by the presence of anterior or posterior asynclitism, but, as a rule, very early in labor these variable degrees of asynclitism are corrected, and the changing axis of the fetal head will indicate that the guiding influence of the lower uterine segment is making itself evident. Providing the uterine forces are strong enough, the head will follow an axis through the true pelvis, which is determined by this latter factor and not by the direction assumed by the fetal axis at

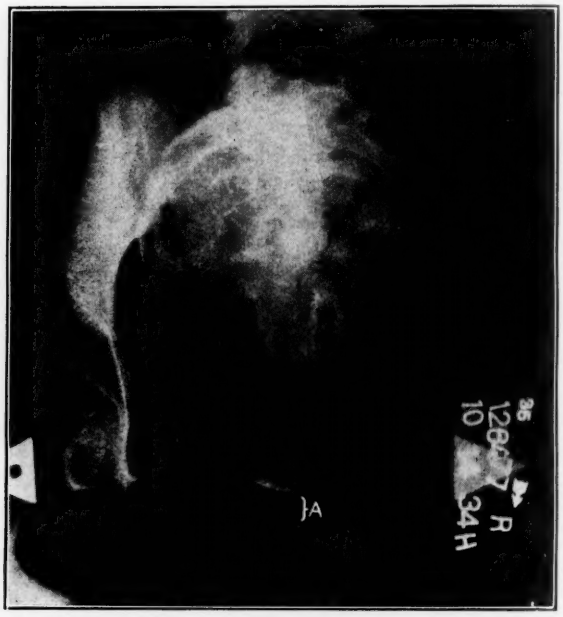

Fig. 2.—The first position of head after descent has occurred in labor. The head is descending through an axis in the fore-pelvis determined by the position of the lower uterine segment. Note the extreme flexion and molding. The anterior part of the head is close to the symphysis "A." Anthropoid type of pelvis. Position of head R. O. A. (Difficult medium forceps delivery, stillbirth.)

the inlet. By the time the cervix is partially dilated, the head in active labor will begin to assume the axis of the lower uterine segment, in which it will ultimately descend to the bottom of the pelvis. The guiding influence of the lower uterine segment and its fascial supporting structures continues to act in determining the axis of descent until the biparietal diameter of the head is in the fully dilated cervix. At this point the stretched fascial supports encircling the head exert their final influence. This terminal effect of the fully dilated cervix on the axis of the descending head can be observed when, prior to a forceps delivery, the last rim of the cervix is manu-

ally pushed over the head. As a result of this maneuver, the axis of the head may be rather suddenly deviated posteriorly from a forward direction.

(B) Variations in the Position of the Lower Uterine Segment

We have noticed that during labor, depending on the direction through which the fetal head is guided by the soft parts, three axes can be recognized. The following three illustrations from roentgenograms, taken after some degree of dilatation of the cervix had been at-

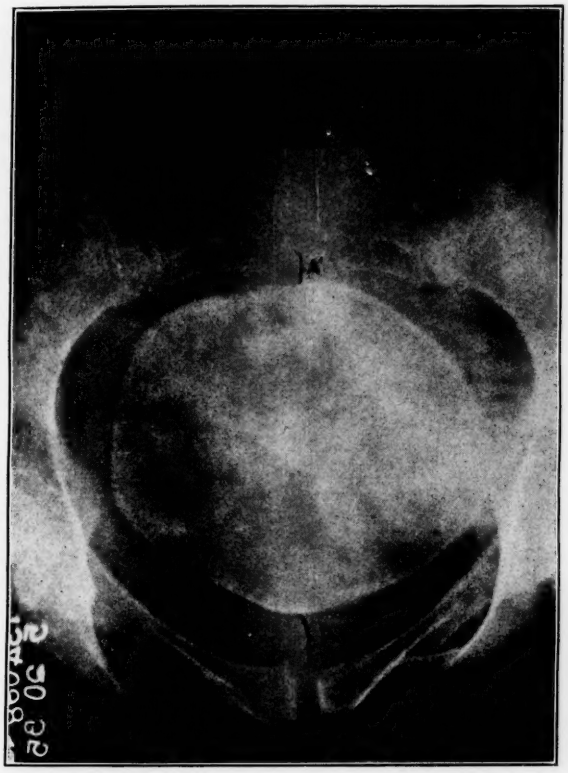

Fig. 3.—The second position of the head after descent has occurred in labor. The head is situated in the mid-axis of the pelvis, slightly favoring the posterior pelvis. (Compare "*A*" and "*A'*.") Position of head L. O. T.

tained, are sufficiently characteristic to reveal the important points. For descriptive purposes these variable positions of the axes, along which the fetal head may descend late in the first stage of labor, may be classified the first, second, and third positions.

In the first extreme example (Fig. 2) the head is situated in the fore-pelvis with the anterior lateral aspect of the head close to the symphysis and descending pubic rami. The posterior lateral portion is considerably removed from the sacrum. Marked molding and flexion of the fetal head are also evident.

In the second position (Fig. 3), the head is centrally situated in the pelvis, theoretically equidistant from symphysis and sacrum, but, as a rule, the head while in this midposition actually tends to encroach more on the posterior pelvis.

In the third position (Fig. 4), the head is situated over the posterior pelvis with the anterior lateral aspect far removed from the symphysis and the posterior portion close to the promontory and sacrum.

These three extreme variations in position of the head may exist at the inlet, but at this high level the position is not of great signifi-

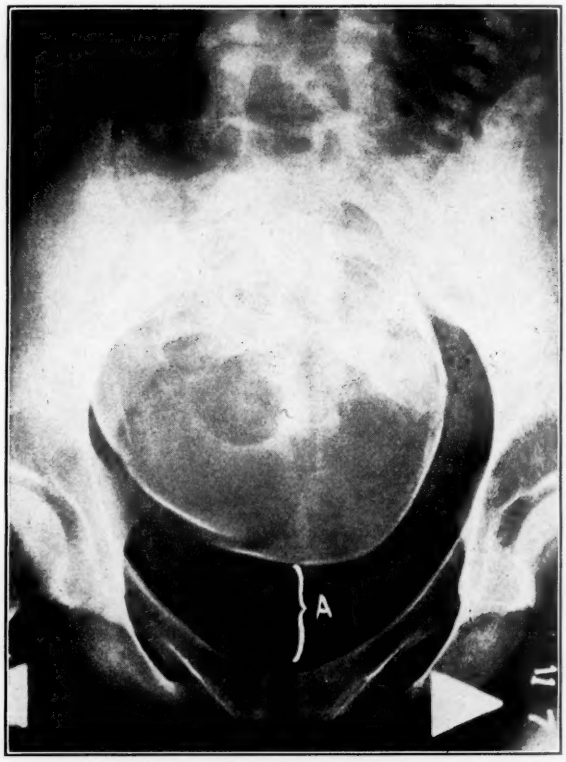

Fig. 4.—The third position of the head after descent has occurred in labor. The head is close to the promontory and sacrum, descending through the axis of the posterior pelvis, as determined by the position of the lower uterine segment. (Note distance from symphysis "*A*.") Position of head R. O. P.

cance. For instance, with the onset of labor the head from any position at the inlet may be forced downward and backward into the posterior pelvis according to the normal mechanism of labor. On the other hand, it may be forced to descend in an axis through the forepelvis; but only a trial of active labor will determine in which direction it will go. It is obvious that the subsequent mechanism in relation to the type of pelvis and the clinical course of labor will be modified by the particular axis of descent which the head is forced to follow.

In view of the fact that we believe the causative factor to be the supporting structures of the lower uterine segment, diagrammatic representations of the supposed appearance of these structures, which would deviate the head into the fore-pelvis or into the posterior pelvis after some measure of cervical dilatation has been attained, are illustrated in Figs. 5 and 6. While it is true that three degrees in the position of the pelvic axis can be recognized, from the standpoint of this investigation only the extreme forward and extreme backward

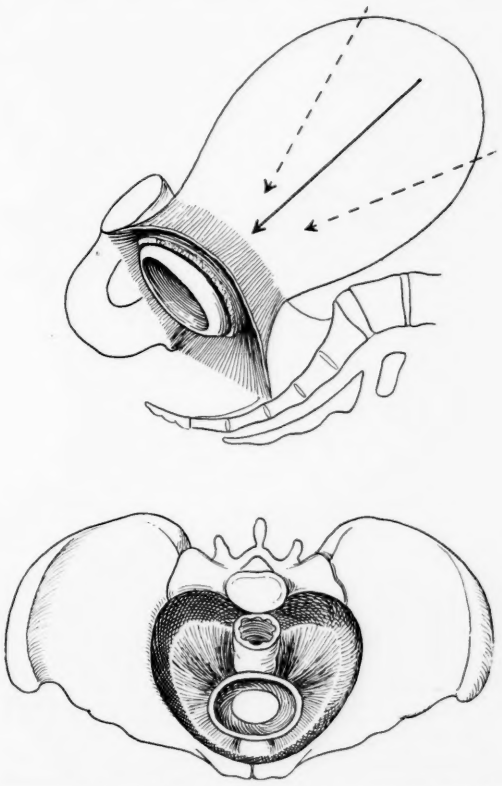

Fig. 5*.—Diagrammatic illustration to show the supposed position of the axis of the lower uterine segment in the fore-pelvis, as caused by the arrangement of the attachments of its fascial supports.

axis of descent are referred to, namely, the first and the third; and we shall now make reference only to the head descending in the fore-pelvis or in the posterior pelvis.

DESCENT OF THE HEAD THROUGH THE FORE-PELVIS

The head, which has descended into the fore-pelvis after partial or almost full dilatation of the cervix has been attained, may have origi-

*The diagrams shown in Figs. 5 and 6 do not indicate correctly the direction of the fascial attachment of the lower uterine segment. The proper direction of these supporting structures is shown in Fig. 1.

nated from such a range of position at the inlet that some attempt must be made to classify the various types and choose representative examples for illustration purposes. For discussion we have chosen the following case types:

1. The type of case in which the head is placed over the fore-pelvis at the onset of labor and descends through and adjusts itself to the particular shape of the fore-pelvis.

2. The type in which at the onset of labor the head is placed over the posterior pelvis where it has already adjusted itself to the particular shape of the posterior

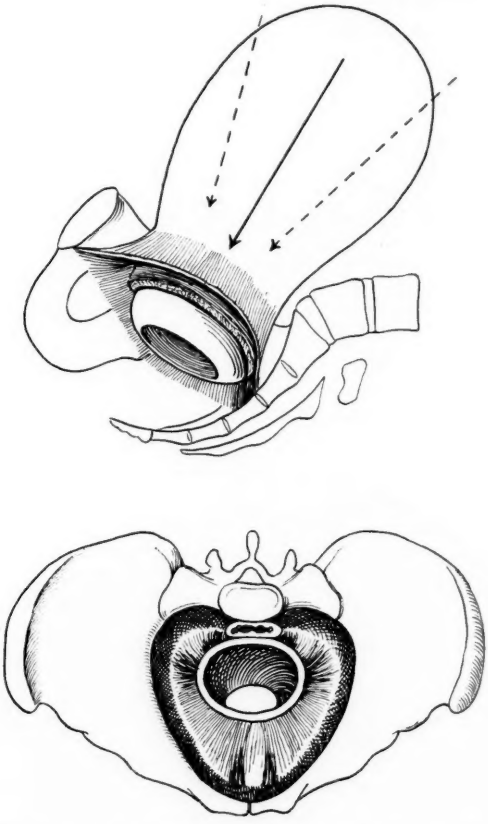

Fig. 6.—Diagrammatic illustration to show the supposed position of the axis of the lower uterine segment in the posterior pelvis, as caused by the arrangement of the attachments of its fascial supports.

segment, only to descend downward and forward during labor, readjusting itself to the shape of the fore-pelvis as it descends.

3. Example of a head directed into and descending through the fore-pelvis, even though the pelvis is normal with a normal inclination, and the child is average in size.

4. The high head in the fore-pelvis which fails to descend either through the fore-pelvis or through the posterior pelvis. Cesarean section ultimately becomes necessary.

(1) Descent and Adjustment to the Fore-Pelvis

We were especially fortunate in obtaining three stereoroentgenograms in the following case study, which demonstrate a number of characteristics of this particular type of mechanism. The type of pelvis corresponds to a fairly typical android with definite narrowing of the fore-pelvis at the inlet, slight convergence of the side walls, and

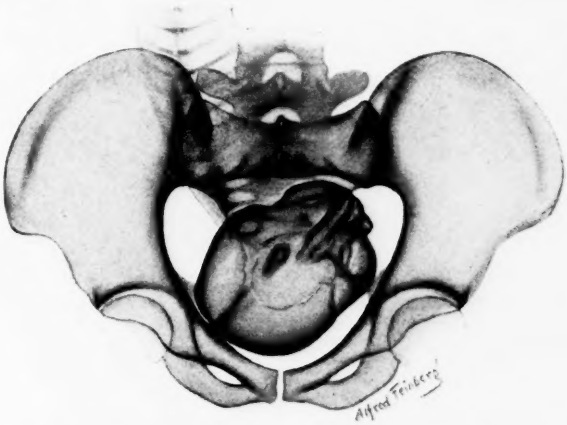

Fig. 7.—First x-ray examination in labor. Head descending through soft part axis situated in the fore-pelvis. Head position R. O. T. Type of pelvis typical android.

Fig. 8*.—Second x-ray examination in labor (same case as Fig. 7). Head descending through soft part axis situated in the fore-pelvis. The head has rotated to the R. O. T.-R. O. A. position.

slight narrowing of the subpubic arch. The first stereoroentgenogram early in labor shows the head over the fore-pelvis in the R. O. T. position (Fig. 7). A later x-ray study shows slight descent with the head now R. O. T. to R. O. A., still more in the fore-pelvis than in the posterior pelvis (Fig. 8). The last x-ray examination (Fig. 9) shows the

*In the succeeding half-tone illustrations with an x-ray effect, the ratio of head size to pelvic size has been modified to show to better advantage the axial position of head to pelvis.

head in the fore-pelvis close to the symphysis and descending pubic rami, almost in the direct O. A. position. When in this position the cervix was four fingers dilated, and the delivery was terminated from this position and level (at or slightly below the level of the spines) by low medium forceps. As a result of the downward and forward axis of the lower uterine segment, we find here an example of adjustment of the head to an anterior position in an android type of pelvis. We have a number of cases showing a pelvis quite similar to this one in size and shape, in which the head descended close to the sacrum in the O. T. position because the lower uterine segment directed the head through the posterior pelvis (see Fig. 17). In fact, this latter mechanism is the more common of the two. The demonstration of these two different mechanisms of labor, in regard to head position

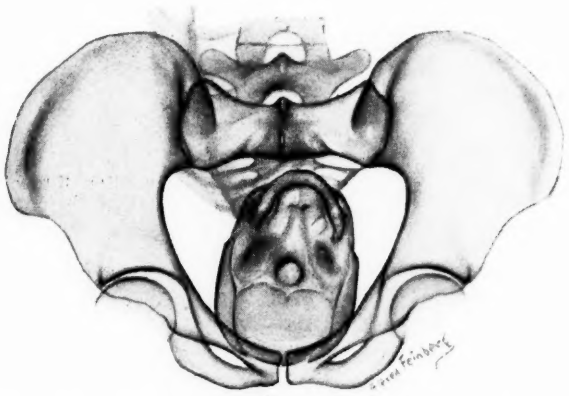

Fig. 9.—Third x-ray examination in labor (same case as Figs. 7 and 8). With further descent through the fore-pelvis the head has rotated almost to a direct O. A. position at the level of the spines.

during descent in the same type of pelvis, indicates the importance of the soft parts in labor. Thus a transverse position in an android pelvis can be predicted only on the basis that this is the more frequent mechanism. In the individual case, as illustrated in Figs. 7, 8, and 9, an anterior position may obtain if the head descends in the fore-pelvis.

Summary of Clinical Course of Labor in This Patient.—Mrs. J. F., white, primipara, aged thirty-five. Unit No. 266285. The patient was admitted to labor room at 7:40 A.M. March 27, 1936, with a history of ruptured membranes since 6 A.M. Pains started at 8 A.M. First x-ray examination at 11 A.M. (Fig. 7). Pelvic examination at 12:35 P.M. showed the cervix to be fingers II, thin, firm. Vertex R. O. T. in brim. Pains every three minutes, lasting thirty to forty seconds. Second x-ray at 4 P.M. (Fig. 8). Pelvic examination at 5 P.M. showed the cervix to be almost fingers III, dilated, thick and firm. Vertex now reported to be slightly anterior. Labor continued during night with pains of moderate intensity. In the

morning the patient was distended with gas. The uterus was deviated to the right. Pains poor in quality. Patient tired. Last x-ray examination at 8:30 A.M. (Fig. 9). Pelvic examination at 10 A.M. disclosed the vertex to be R. O. A. and showed the cervix to be fingers IV, dilated, and a thick rim remaining. Delivery by medium forceps at 4:47 P.M. March 28. Vertex direct O. A. in fore-pelvis at level of spines. Patient was in shock, requiring infusion and, several days later, a transfusion. Weight of child: 3430 gm. Duration of labor: thirty-four hours.

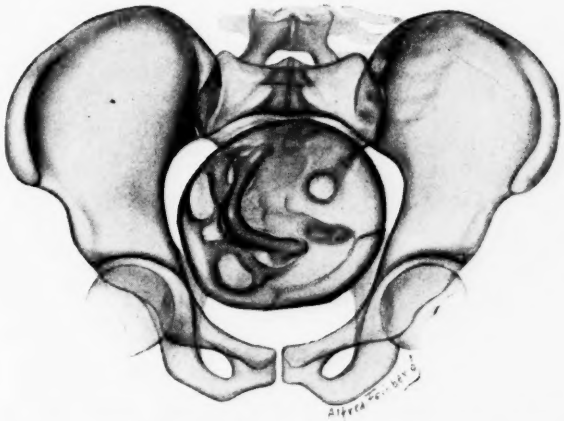

Fig. 10.—First x-ray examination early in labor shows vertex L. O. P. situated over posterior pelvis. Type of pelvis android with anthropoid characteristics.

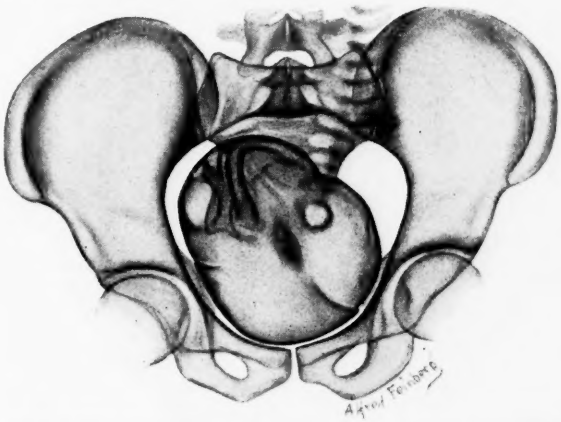

Fig. 11.—Second x-ray examination later in labor (same case as Fig. 10). The fetal head has been carried forward and downward into the fore-pelvis by the influence of the position of the lower uterine segment. As it is carried into the fore-pelvis, close to the symphysis, it has adapted itself to the narrow fore-pelvis by rotating to the L. O. A. position.

(2) Descent Through Fore-Pelvis From a Primary Posterior Pelvis Position at the Inlet

We have a number of case studies to illustrate this interesting type of axis of descent through the fore-pelvis and its resultant effect on the mechanism of labor in relation to pelvic type. The pelvis conforms

to the android type with anthropoid characteristics, in which definite transverse narrowing exists throughout the pelvis and a long, narrow fore-pelvis is present. The first roentgenogram (Fig. 10) obtained in labor showed the head engaged in the L. O. P. position and situated over the posterior pelvis. This is the ideal position for the head at the inlet in this particular type of pelvis. The second roentgenogram obtained in labor, however, shows a very different fetal-pelvic relationship (Fig. 11). The head is now close to the symphysis and pubic rami, far removed from the mid and lower sacral region in the L. O. A. position. In other words, the head has descended downward and forward along an axis which carries it away from the posterior pelvis into the fore-pelvis and so prevents it from utilizing the maximum space posteriorly. Normally, such deviation of the axis anteriorly should not occur until the head has passed through the

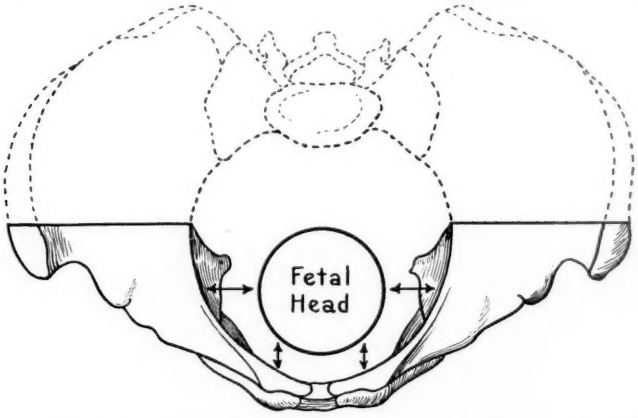

Fig. 12.—Diagram to illustrate that a head carried through the fore-pelvis by virtue of a forward axis of the lower uterine segment will attempt to adjust itself to the shape of the bony boundaries of the fore-pelvis.

cervix. To compensate for this change in axis of descent, the head must now adapt itself to the shape of the bony walls of the fore-pelvis.

Clinical Course of Labor.—Mrs. K. C. (Unit No. 448977), white, primipara, aged twenty-four. Weight of baby: 3600 gm. The patient was admitted at 6 A.M. July 2, 1935, with a history of uterine contractions since 3 A.M. The vertex was engaged on admission. Pains increased in frequency and severity. First x-ray examination at 9:20 A.M. (Fig. 10). Pelvic examination at 11:30 A.M. revealed a narrow rim of cervix remaining; membranes ruptured. Position L. O. T. The head was pushed against the symphysis with plenty of room in hollow of sacrum. Second x-ray examination at noon (Fig. 11). The labor was terminated at 3:30 P.M. by low medium forceps after failure to advance with adequate second stage contractions. Duration of labor: twelve and one-half hours.

We believe these two case studies (Figs. 7 to 11) demonstrate certain principles in regard to fetal head adaptation during descent as

well as in the variation in the pelvic axis through which the fetal head descended. The principle, to a certain extent, is illustrated in Fig. 12, which indicates that when a fetal head is forced to descend through the fore-pelvis it must attempt to adjust itself to the particular shape of the fore-pelvis. We have a number of similar examples, in which the head adjusted itself during labor from some other position at the inlet to a direct O. P. position lower in the fore-pelvis as it was guided downward and forward through the axis of the lower uterine segment. In such cases, the pelvis usually conforms to an anthropoid type with a narrow fore-pelvis.

(3) Fore-Pelvis Descent Through a Normal Pelvis

The case studies just described possessed pelves of abnormal size and shape, and as a result the pelvis itself may be supposed to have

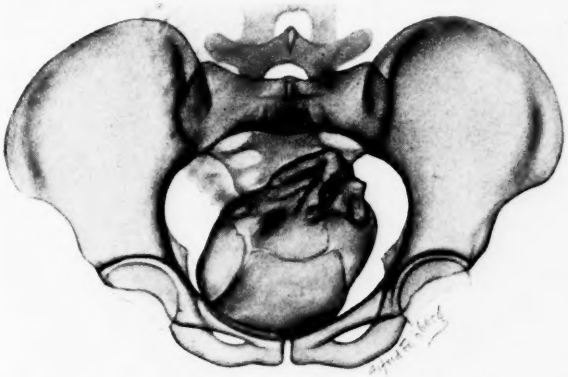

Fig. 13.—A good example of a head directed downward and forward by the lower uterine segment against the symphysis into the fore-pelvis. The pelvis is normal. No fetal-pelvic disproportion is present. The inclination of the pelvis is normal.

modified the course of the head in association with a downward and forward fetal piston axis. We were fortunate in obtaining the example shown in Fig. 13, which would seem to give further support to the theory that the position and direction of the axis of the lower uterine segment is determined by its fascial attachments to the pelvic side walls. The pelvis conforms to the normal or gynecoid type. The inclination of the inlet is normal. The roentgenogram illustrates that the anterior parietal aspect of the fetal head is quite close to the posterior aspects of the symphysis and that a large space exists between the posterior lateral aspect of the head and the lower sacral region. It is true that the axis of the fetus is pointing downward and forward, and, theoretically, such an attitude might be regarded as the sole cause for the position of the head in relation to the pubes. It is hard to believe, however, in a pelvis of such ample dimensions that fetal

axis alone would prevent the head from making use of the spacious posterior pelvis. The labor was prolonged and complicated by inertia and slow cervical dilatation. The delivery was terminated by a low medium forceps operation.

Clinical Course of Labor.—Mrs. F. B. (Unit No. 476830), white, primipara, aged thirty-four. Weight of child: 3550 gm. Length of labor: twenty-seven hours. The patient was admitted to labor room at 8:30 P.M. Aug. 11, 1936, with history of pains since 12:15 A.M. Pelvic examination at 11:15 P.M. shows the cervix to be fingers II, dilated and thin. Vertex near spines, R. O. T.; membranes ruptured. Moderately severe contractions continued during the night and the following morning. X-ray (Fig. 13) examination was obtained about 10 A.M. August 12. Pelvic examination at 1:15 P.M. showed the cervix to be fingers III to IV, dilated. The anterior lip of the cervix was firm. Vertex in fore-pelvis (No. 1 position) R. O. T. Marked caput

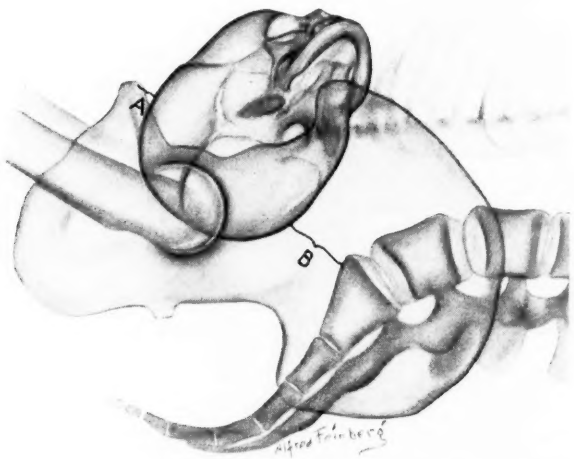

Fig. 14.—X-ray examination obtained during trial of labor. Head is high, held against symphysis. (Compare the lengths of *A* and *B* with similar distances shown in Fig. 19.) Cesarean section.

and molding at level of spines. Pains occurring every two or three minutes. With cervix out of the way and the vertex R.O.T., the patient was delivered by low medium forceps at 5:20 P.M.

(4) The High Head in the Fore-Pelvis Which Fails to Descend

A study of the roentgenograms obtained during a trial of labor, in which the delivery was accomplished later by cesarean section, illustrates several important points which may or may not be attributed to the position of the lower uterine segment. In Fig. 14 the head is high over the fore-pelvis close to the symphysis and abdominal wall. It is true that there is disproportion in conjunction with an abnormal pelvis in this case, but, from our own clinical experience, we believe that this high head, to a certain extent, is held forward by tense fasciae which

maintain the head in a poor mechanical situation for descent and that, had the same head in the same pelvis been permitted to occupy a position over the posterior pelvis at the beginning of labor, delivery from below might have been possible.

We have pointed out that the upper portion of the lower uterine segment is not controlled by fascial attachments to the same degree as its lower portion (Fig. 1). To assume that tense fasciae may hold a floating head against the symphysis at the inlet would require an associated high level for the uterocervical junction ("*X*," Fig. 1), from which the supporting structures originate.

From these observations it would seem that such variations in the level of the cervix must exist, due to the fascial supports themselves; but further investigation is necessary to prove this point.

DESCENT THROUGH THE POSTERIOR PELVIS

As in the analysis of examples of descent through the fore-pelvis, case studies can be found to demonstrate great variation in the extent to which the fetal-pelvic relationship must change before the head ultimately descends in a posterior axis in relation to the sacrum and shape of the posterior pelvis. Comparable types of cases discussed under descent through the fore-pelvis may be chosen.

1. Descent from inlet to outlet through the posterior pelvis and associated adjustment to the shape of the posterior pelvis.

2. Descent through the posterior pelvis from a primary position high over the fore-pelvis.

3. The efficient course of labor in normal pelves, with a child of average or under average size, when descending through the posterior pelvis.

4. The favorable prognostic sign of a head high, but situated over the posterior pelvis.

(1) Descent From Inlet to Outlet Through the Posterior Pelvis

The shortest and easiest axis for the head to follow when situated at the onset of labor over the posterior pelvis is that through the posterior pelvis. An example has already been given in Fig. 4, where it will be observed that the fetal head is descending in a large anthropoid type of pelvis in the R. O. P. to R. O. T. position, close to the promontory and sacrum. The labor was uncomplicated, except for an outlet forceps delivery. Precisely the same axis is being followed in the example shown in Fig. 15. The pelvis in this case conforms to the typical android with a gynecoid fore-pelvis. The head, revealing extreme flexion and molding, is descending in the R. O. T. to R. O. P. position, close to the sacrum and as far removed from the posterior aspect of the symphysis as it is mechanically possible to be. In this case, in spite of a large child (8 pounds) and a small abnormal pelvis,

the vertex descended rapidly through the pelvis to bulge the posterior perineal region. After failure to advance beyond this low level, labor was terminated by forceps. Under these circumstances the influence

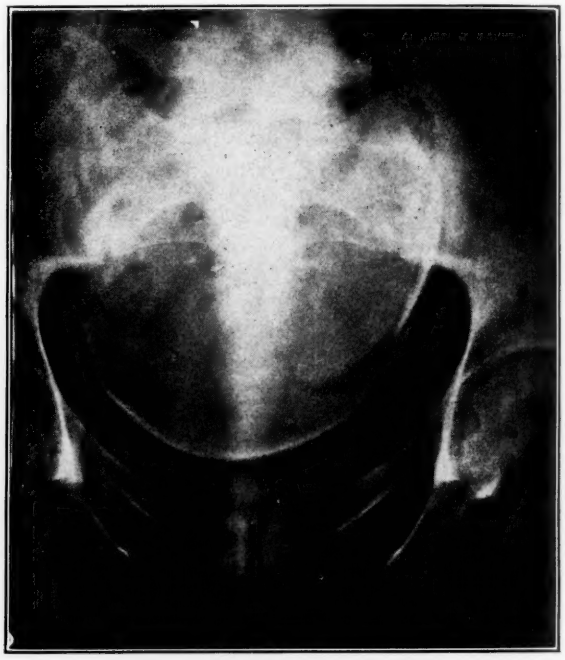

Fig. 15.—Anteroposterior roentgenogram showing the head, R. O. P.-R. O. T. position, descending through the posterior pelvis as far removed as possible from the symphysis, *A*. Type of pelvis android.

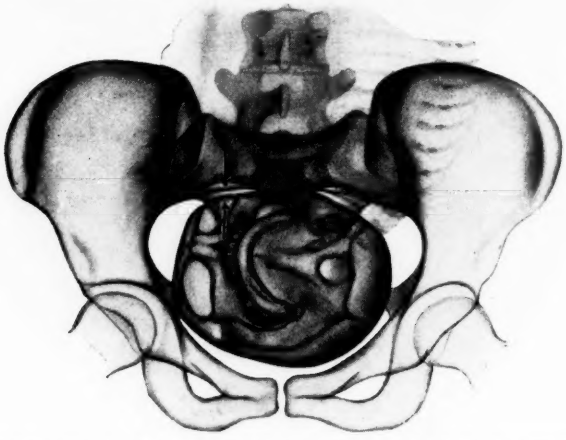

Fig. 16.—Mechanism in the android type when the head is directed through axis of the posterior pelvis. The head is in the O. T. position and, as a rule, maintains this position to a low level as a result of the shape of the posterior pelvis.

of the type of pelvis upon head position during descent through the posterior pelvis becomes apparent. In other words, when the head is

forced to follow the axis of a lower uterine segment situated in the posterior pelvis by virtue of the length, strength, and character of its fascial supports, the head will attempt to adjust itself to the shape of the posterior pelvis as it descends (Fig. 16).

Last year we discussed this particular result on the mechanism of labor and described the mechanism in android types according to the principles illustrated in Fig. 17. In anthropoid types, when the head engages and descends in the oblique posterior position through the axis of the posterior pelvis (Fig. 4), rotation to the anterior position usually does not occur until the head is through the cervix and meets the resistance offered by the lower posterior aspect of the pelvic gutter. Thus when we observe the head descending in the posterior pelvis, the type of which is known, we can understand the reasons for expecting transverse positions in android types, and posterior positions in

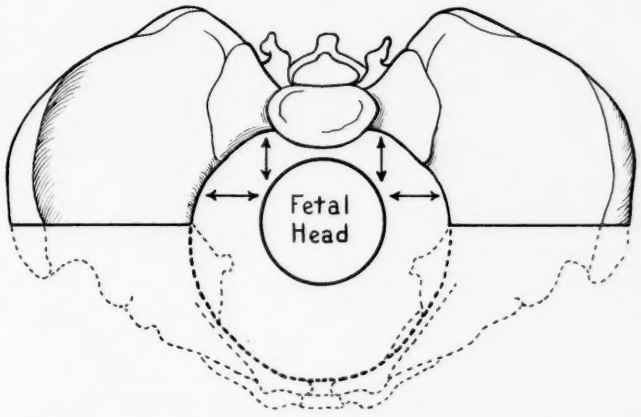

Fig. 17.—Diagram to show that, if the head is directed through the posterior segment of the pelvis by the position of the axis of the lower uterine segment, it will adjust itself to the shape of the posterior pelvis. Hence, transverse positions are common in android types, and posterior positions in anthropoid types.

anthropoid types; and we can also understand why, as a result of fetal-pelvic adaptation to the shape of the posterior pelvis, the head may not be rotated at the level of the spines with ease in the android type, but must be brought to a lower level before rotation can be effected; or why in the anthropoid type of pelvis the posterior position may be difficult to rotate until it has descended through the cervix.

(2) Descent Through the Posterior Pelvis From a Primary Position High in the Fore-Pelvis

In contrast to cases of descent through the fore-pelvis from a primary position higher in the posterior pelvis, we have encountered examples in which the head was originally directed into the fore-pelvis, but later in labor was forced to descend in an axis determined

by the axis of the dilating lower uterine segment, which showed a downward and backward curve. A representative example is shown in Figs. 18 and 19. Early in labor (Fig. 18) the head presented high, close to the symphysis in the L. O. T. position, with a definite posterior parietal tendency and with the long axis of the fetus directed downward and forward. The second x-ray examination, obtained when the

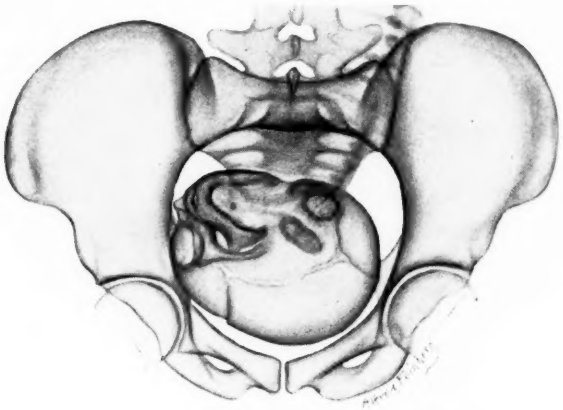

Fig. 18.—X-ray examination early in labor. Vertex L. O. T. posterior parietal position situated over fore-pelvis.

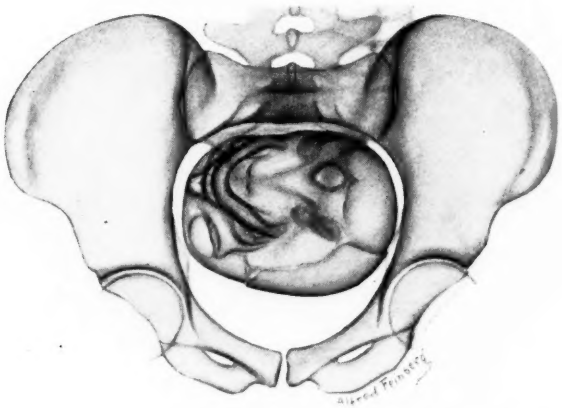

Fig. 19.—Second x-ray examination later in labor (same case as Fig. 17) shows vertex has been carried away from symphysis into the axis of posterior pelvis by means of the influence of the lower uterine segment.

cervix was fingers III to IV, dilated (Fig. 19), shows that the downward and forward axis of the fetus, as a whole, still persists, although to a lesser degree, and that the entire head is now more removed from the symphysis and is situated nearer to the posterior pelvis. A long labor was necessary to permit the head to descend slowly, more and more into the axis of the lower uterine segment situated in the posterior pelvis. Because of lack of satisfactory progress the patient was

placed on the delivery table with the cervix thinned out and four fingers dilated. As soon as the bi-parietal diameter of the head passed through the cervix, it laterally flexed into the posterior pelvis close to the sacrum in its proper axis for further descent.

Clinical Course of Labor.—Mrs. A. M., white, primipara, aged twenty-three. Weight of child: 3270 gm. Duration of labor: fifty hours. The patient was admitted to the labor room at 11:30 P.M. Sept. 10, 1935. Pains began at 10 P.M. with slight show. On admission contractions occurred every fifteen to twenty minutes, lasting thirty or forty seconds. Pelvic examination at 10:30 A.M. showed the cervix to be fingers I dilated, thick, effaced. First x-rays at 10:50 A.M. (Fig. 18). Pains increased in frequency. Pelvic examination at 1 A.M. September 12 showed the cervix to be fingers II dilated and thick; membranes intact. Pelvic examination at 9 A.M. September 12 showed the cervix to be fingers IV. Second x-ray examination at 10 A.M. September 12 (Fig. 19). Pelvic examination at 11 A.M. revealed the cervix to be thin, and fingers IV dilated. Delivery by low forceps at 2:57 P.M. September 12. Head at spines, vertex L. O. T. Sagittal suture pointing into the fore-pelvis. Thin rim of cervix. As the cervix was pushed over the head the vertex laterally flexed into the posterior pelvis and was rotated manually at a lower level to an O. A. position.

(3) The Efficient Course of Labor in a Normal Pelvis With Descent Through the Posterior Pelvis

In a recent publication[1] we discussed fully the normal mechanism of labor and pointed out that the head normally is directed downward and backward, more through the posterior pelvis than through the mid- or fore-pelvis. As a result of the soft parts directing the head more commonly in this posterior axis, we were able to associate anatomically this common soft part axis with the bony pelvis. For practical purposes this soft part axis corresponds to a line descending parallel with the sacrum from the points of intersection of the widest transverse diameter and the anteroposterior diameter at the inlet. Although labor, as a rule, is efficient when such an axis is followed, a number of exceptions have been noted in which the labor is complicated by inertia and cervical dystocia, and an operative delivery may become necessary. We have observed that at the onset of labor the head may have already descended to a low level in the pelvis in an ideal axis for further descent in the axis of the posterior pelvis. Such a case is illustrated in Fig. 3. Yet, during labor, the cervix dilated slowly and inertia was present. The delivery was terminated by manual dilatation of the cervix and a low median forceps operation. The presence of a normal pelvis and engagement of the head in similar examples rule out the possibility of disproportion. This type of case is not uncommon. We have observed, however, that the head is frequently large and round. The explanation for the cause of the diffi-

culty with the cervix is not clear, but it would seem that the fascial supports, although maintaining the head in a good position, prevent it from effectively distending the lower uterine segment to "get at the cervix."

(4) The High Head Held Over the Posterior Pelvis as a Favorable Prognostic Sign

Occasionally the floating head causes considerable concern early in labor, whether or not the patient is known to have a normal or abnormal pelvis. If, however, it is held close to the sacral promontory, as illustrated in Fig. 20, a longer trial of labor is justifiable, because it is situated over the posterior pelvis in an ideal position for descent,

Fig. 20.—The fetal head, though floating, is situated close to promontory over the posterior pelvis in the ideal position for descent through the posterior pelvis. Favorable prognostic sign. (Compare the lengths of *A* and *B* with similar distances shown in Fig. 14.)

provided, of course, the soft parts are so disposed as to maintain this axis throughout the posterior pelvis as the head descends.

FREQUENCY OF OCCURRENCE OF THESE VARIATIONS IN AXIS OF FETAL DESCENT

In view of the fact that considerable experience is necessary on the part of the observer in order to appreciate correctly, in the stereoscopic image of head and pelvis, the axis of fetal descent in relation either to the symphysis in front or the sacrum behind, we considered at one time that the descent through the fore-pelvis was rare in occurrence, and that in the vast majority of all cases the descent was eventually through an axis in the more ample posterior pelvis. However, when

we reviewed films obtained during the investigation of related aspects of the mechanism of labor and became more experienced in the study of fetal-pelvic relationships, we began to find that varying degrees of descent through the mid- or fore-pelvis occurred with greater frequency than we had suspected.

At this time, however, we have made no statistical analysis of our series possessing one or more stereoroentgenograms obtained in labor, and we hesitate to suggest the frequency with which the head may be directed downward through the fore-pelvis. Yet, it is of sufficiently common occurrence to be taken into account in each case of prolonged labor, because, as the histories indicate, the clinical course of labor in these cases appears to be complicated by inertia, cervical dystocia, and prolonged labor. Manual dilatation of the cervix, followed by a forceps delivery, is not an uncommon method of terminating the labor in these cases.

In conclusion, although the roentgenologic and clinical data must be correlated with great care in a larger series of cases, we believe that a knowledge of the axis of descent is essential before the proper treatment can be instituted. Earlier recognition of these variations in labor by either roentgenologic or clinical methods of diagnosis, or both, will enable us to institute the proper treatment early in labor, in an attempt to avoid exhaustion of the patient and the difficult operative deliveries which are so frequently necessary in these cases.

SUMMARY

1. The lower uterine segment and its fascial supports represent an active force in determining the axis along which the fetal head must descend through the pelvis.

2. The maximum guiding influence of the lower uterine segment becomes evident only after definite dilatation of the cervix has occurred.

3. The position of this axis is variable in each individual case, and examples of descent through the fore-pelvis, the mid-pelvis, and the posterior pelvis are described.

4. The clinical course of labor and the head position in relation to pelvic type is distinctly modified, depending on the particular axis the head follows.

5. In the majority of instances, roentgenologic diagnosis cannot be made dogmatically during labor, because only the active forces of labor can ultimately determine the axis through which the head can descend. The later the examination is taken, the greater the possibility of accurately determining the axis the head is attempting to follow.

6. These variations in labor in the fetal axis of descent, we believe, will ultimately enable us to understand the question of inertia and cervical dystocia, and the correct method of treatment for these conditions.

7. A knowledge of the possible occurrence of these variations in any individual case in labor is essential before a reliable clinical and roentgenologic diagnosis can be made.

8. Patients who are not progressing normally in labor warrant a careful examination in order to determine, among other things, if the head is descending in the proper relation to the symphysis in front or the sacrum behind.

9. The variability of the fetal axis of descent with its resultant effect on the mechanism of labor indicates that difficulty in labor cannot be anticipated by linear or volumetric measurements alone.

10. The mechanism of labor in relation to the shape of the pelvis cannot be adequately discussed without taking into account the variations in the position of the axis of the lower uterine segment, along which the head descends.

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875 Park Avenue

DISCUSSION

DR. E. D. PLASS, Iowa City, Ia.—I must confess that I find some difficulty in following the arguments of the authors.

It is quite easy to agree with the first point brought forward, namely, that the posterior parietal bone presents earlier than the anterior, but I am inclined to believe that such a phenomenon is associated with some distortion of the bony pelvis rather than with abnormalities of the soft parts. It is obvious that if the pelvic inclination is increased, there would be a tendency for the posterior parietal to descend first, and we have long recognized that in patients showing even slight disproportion there is a tendency in the same direction. I find it very difficult to think of soft tissues altering the position of the head and am rather inclined to the opinion that the position of the soft parts, that is of the lower uterine segment, is more likely to be determined by the configuration of the bony canal. There are several arguments that seem to support such a contention. For example, it is recognized that a patient with unilateral lameness has probably a distortion of the pelvis with one oblique diameter longer than the other, and it has been almost a universal experience that the head enters the pelvis in the long diameter. The head accommodates to the change of the bony pelvis irrespective of the soft parts.

Some of the slides that Dr. Caldwell has shown are difficult to interpret because of the lack of definite knowledge as to the situation of the head. I gathered the impression that the distance between the head and the symphysis may well depend upon the situation of the head; that as the head is engaging it might have come

closer to the sacrum or to the symphysis, whereas after descending into the pelvis there would be a tendency for closer approximation to both the anterior and posterior walls.

The arguments that were advanced in the paper, but were not included in the spoken presentation, concern in part the possible activity of the uterosacral ligaments and I gained the impression from going over the manuscript that Dr. Caldwell feels that those ligaments are contractile in nature. The general teaching is that the uterosacral ligaments are merely folds of connective tissue, and that being the case, it is difficult to understand how they can in any way actively influence the position or shape of the lower segment and thus influence the position in which the baby enters the pelvis.

There has developed a fairly wide appreciation of the fact that under the influence of the changes induced by pregnancy all malpositions of the uterus, including both the cervix and the body, tend to disappear. We are familiar with the fact that the retroverted pregnant uterus usually cannot be differentiated in three or four months from the uterus that started pregnancy in the anteverted position. That susceptibility of the uterus to alterations in its position makes me very skeptical of its having such influence upon the position of the head during labor.

DR. ALBERT H. ALDRIDGE, NEW YORK, N. Y.—At the Woman's Hospital we have had no actual experience in studying the mechanism of labor by the Caldwell method. However, I would like to call attention to certain commonly observed facts which seem to suggest that it is almost impossible, during labor, for the fascial supports of the uterus so to fix the position of the lower uterine segment in the anteroposterior diameter of the pelvis, as to constitute an important factor in directing the course of the fetal head.

From the anatomical standpoint, it is agreed quite generally that the uterus is supported by a layer of endopelvic fascia referred to as the upper pelvic floor. In the base of each broad ligament this fascia is thickened to form the so-called cardinal ligaments which are attached to the uterus at the level of the internal os. These ligaments extend laterally and provide the chief support for the uterus. That portion of the endopelvic fascia extending between the uterus and the inner surface of the anterior border of the pelvis is looked upon as the weak portion. Posteriorly the upper pelvic floor is composed of a layer of endopelvic fascia and the uterosacral ligaments.

Undoubtedly, as Dr. Caldwell has pointed out, the position of the cervix in relation to the sacrum and symphysis pubis varies slightly in different women. If the cervix were held in this fixed position, during labor, it is conceivable that it might be a factor in directing the course of the fetal head.

It is known that any relaxation of the endopelvic fascia supporting the uterus, and especially the cardinal ligaments, results in great mobility of the uterus and in some degree of uterine prolapse. When the cardinal ligaments are shortened, even as little as 1½ to 2 cm., on either side, by the Donald-Fothergill operation, a prolapsed uterus, with cervix presenting at the vaginal introitus, can be restored to a normal position.

As the cervix dilates at the level of the internal os during labor, it is obvious that the fascial supports of the uterus which are attached at this level must relax, allowing increasing mobility of the lower uterine segment. When the cervix has reached full dilatation, it practically lines the true pelvis, causing complete relaxation in every direction of all the fascial supports of the uterus, allowing great mobility of the lower uterine segment. This undoubtedly is nature's protective mechanism which prevents injury of the fascial supports of the uterus during labor.

At the end of the third stage of labor, there is so much mobility of the uterus that the cervix frequently presents at or protrudes through the vaginal introitus. If under such circumstances the uterus is replaced manually to a normal level, it will

be found that the cervix can be easily moved to any position in the true pelvis. As the cervix closes during involution, normal tension is restored to the fascial supports of the uterus. As a result, a uterus which seems definitely prolapsed at the end of labor will invariably be found in normal position when involution is completed.

Therefore, in view of the facts presented, it seems doubtful as to whether the lower uterine segment remains sufficiently fixed in position, as labor progresses, to constitute an important factor in directing the course of the fetal head.

DR. HUGO EHRENFEST, ST. LOUIS, MO.—Caldwell's careful x-ray observations have established marked variations in the proximity either to symphysis or sacrum of the axis along which the head descends into the pelvis. According to his view, the unfavorable approach toward the symphysis on the one hand, and the more favorable deviation of the head backward toward the sacrum on the other, are determined by certain anatomic conditions of the fasciae supporting and stabilizing the cervix. It seems to me that his contention is well supported by certain observations we make in vaginal examinations, during labor. We find in one case the dilating os close to the symphysis with a broad, distended posterior cervical lip, and discover in another case just the opposite situation with the os far back in the posterior fornix. If I understand the essayist correctly, these variations would have to be considered to be of great prognostic significance.

I am wondering whether Dr. Caldwell, on the basis of his information concerning the fixation of the cervix in relation to either the anterior or the posterior pelvic wall, is willing to support my own idea of the occasional fixation of the cervix at an unusually high level in the pelvis. I assume this condition to be present when in a primigravida with a normal pelvis, a seemingly normal, flexed head fails to become engaged either late in pregnancy or even with beginning cervical dilatation in labor. We all have observed cases in which such an unengaged head with complete dilatation of the cervix and rupture of the membranes rather quickly descends into the pelvis. Many an unjustifiable cesarean section has been done under such conditions, because failure or rather impossibility of the head to enter the inlet had erroneously been ascribed to a disproportion.

DR. LILIAN K. P. FARRAR, NEW YORK, N. Y.—The supports of the uterus have received many different names, "the parametrium," "the broad ligaments," "the cardinal ligaments," "the sustentacular apparatus" of Bonney, and perhaps the most inclusive name, "the upper pelvic floor" by Polls. The best description, however, I believe, is that given by Mackenrodt in 1894 ("ligamentum transversalis colli"), who described a triangular wedge of tissue on either side of the cervix made up of thick bundles of muscle and connective tissue passing from the sides of the pelvis into and down the sides of the cervix and vagina and extending anteriorly from either side of the rectum up to and under the bladder. This "ligament" Mackenrodt held to maintain the uterus in anteflexion. I believe that Dr. Caldwell is correct in assuming that these fascial attachments of the lower pole of the uterus influence the fetal head in its descent through the pelvis.

DR. BENJAMIN P. WATSON, NEW YORK, N. Y.—I would like to say that Dr. Caldwell and his associates are approaching this subject in a most critical fashion. I have been one of their chief critics. Their evidence is becoming so great in the type of pelvis to which Dr. Caldwell has applied these investigations that I am a convert to the idea that the soft parts do play a considerable part in a great many dystocias.

DR. CALDWELL (closing).—The mechanism of labor as shown in the first slide is the usual mechanism which we have found in a very careful and rather critical examination of over 250 primipara cases. It is very difficult to see what else would tilt the child's head toward the symphysis or carry it backward toward the center of

the pelvis except the shape and the support of the lower uterine segment. It is difficult to see a very small head held close to the sacrum in a very large anthropoid pelvis where we cannot find any bony obstruction and explain it on a basis of bony disproportion. Undoubtedly bony disproportion would hold the head up, but in the cases where x-ray shows no bony disproportion it is difficult to explain it in any other way except by the soft parts. A great many cases that are held close to the symphysis dilate the cervix up to two or three fingers' dilatation and on rectal examination you can find a good deal of space between the posterior parietal bone and the sacrum, and with each drive it is pushed forward into the pelvis. Ultimately this is corrected and in subsequent pregnancies the labor must be very much easier. It would be well if the Society would investigate this subject during the coming year and see whether we are right or not.

A CLINICAL REVIEW OF 110 CASES OF OVARIAN CARCINOMA*

FRANK W. LYNCH, M.D., F.A.C.S., SAN FRANCISCO, CALIF.
(From the Department of Obstetrics and Gynecology, University of California.)

THE diagnosis of tumors is not always easy. It is one thing to outline the mass but quite another matter to determine its nature when the patient is difficult to examine, or complications are present. A review of tumors treated recently in my clinic showed that 5.6 per cent of 300 fibroids were not recognized as such preoperatively, nor were 15 per cent of 302 ovarian neoplasms recognized as ovarian. Follicle and corpus luteum cysts were not included in the group because they are not true neoplasms. In addition to these errors, there were at least as many "correct and incorrect" diagnoses, which term we used when a fibroid or ovarian cyst associated with some other pelvic condition was present and diagnosed but the associated condition was not, or when the likely possibilities of the mass alone were listed with arguments for and against each proposal, but without definite conclusions. The net result of this study showed an absolutely correct diagnosis in less than 90 per cent of 300 fibroids, and in only 64 per cent of 302 true ovarian neoplasms.

The importance of determining the exact nature of any tumor preoperatively needs no discussion. Thirty-six per cent of the 302 ovarian neoplasms under study proved carcinomatous, while cancer occurred in the uterus or tumor in two and a half per cent of 1,200 fibroids. Errors in diagnosis of ovarian tumors assume added importance because the improvement in results attending the present-day treatment of cervical cancers and of cancers of the uterine body has not yet been obtained with ovarian carcinoma. These reasons influence me to pre-

*Read at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 28, 1936.

A study made possible by the Cancer Fund of the University of California.

sent this clinical review of 110 ovarian cancers, all of which have been followed from treatment to death or to a survival as long as nineteen years.

MATERIAL

The material consists of 110 proved carcinomas, all primary growths, except two Krukenberg tumors. Excluded from this series are several carcinomas which were secondary to cancer primary in the uterus, also several secondary sarcomas.

The series comprises 95 papillary and/or adenocarcinomas, 5 malignant pseudomucinous tumors, 1 squamous cell carcinoma arising in a dermoid, 1 disgerminoma, 6 granulosa cell tumors, and the 2 Krukenberg tumors which were considered primary ovarian tumors before operation, and gave no clear history of the stomach cancer until after the tumors had been removed. Sixty-five of the entire group were bilateral, and 45 were unilateral tumors. Checkup of the histories of the 45 unilateral tumor patients showed that one ovary had been removed by operation in nine of them a few years before the beginning of the present illness. Sixty of the papillary and adenocarcinoma group were double, and 35 were unilateral tumors. Two dermoids were found in ovaries which were the seat of adenocarcinoma. These dermoids, however, were not involved in the malignancy.

The 110 ovarian carcinomas constituted 36 per cent of 302 ovarian neoplasms, 13.3 per cent of 825 pelvic cancers in women, and 4.8 per cent of 2,300 pelvic neoplasms treated in the University of California Hospital from 1916 to date. The microscopic findings in 17 of the papillary adenocarcinomas indicated that they originated in a previously benign papillary adenoma. All of them contained areas which showed irregular proliferation of epithelial cells, mitotic figures, hyperchromatism, obvious invasion of the stroma, and round cell infiltration surrounded by areas of benign tumor formation. To these 17 malignant cases we must add another, although the microscopic findings indicated that it was benign. It recurred, however, a few months after what was considered a complete removal of the tumor, the opposite ovary, and the uterus. Nor did it regress after roentgen ray therapy but caused ascites and death within sixteen months.

FAMILY HISTORY

The part that inheritance of susceptibility to cancer (or failure to inherit resistance to it) plays in the etiology of cancer is a moot question which cannot be proved or disproved at present, either by clinicians or by eugenists, who are as divided in their opinions as we are ourselves.

Cancer now is the second most common cause of death noted in Bureaus of Vital Statistics. Accordingly, patients when intelligently questioned should report cancer in their family history, provided the medical history of many of their blood relations is known to them. A positive history of cancer in the family was given by 42 of the 110 ovarian patients (40 per cent), although no women knew the medical history or death causes of any great-grandparents, only 18 knew similarly of one or more grandparents, only 23 knew such facts concerning both parents, and one knew only the cause of death of one parent (cancer of the bowel). It is of interest that the mothers of 15, and

the fathers of eight of the 42 women with a positive family history actually had cancers themselves. Only one patient, a girl of twenty-two, knew of two deaths in the family from cancer. Her father died of cancer of the leg, and his sister, when quite young, died also of cancer.

A study of the duration of the disease from the time of first symptoms showed practically identical survival curves in the group which had a positive history of cancer in the family, and in those which did not.

No other group of pelvic cancers studied in my clinic have given such a high percentage of positive family history, although, of course, 110 cases are far too few to afford any definite data. However, as controls, we have studied the family history of a number of women who had been operated upon for various gynecologic complaints other than cancer. A positive history of cancer in the family was given in 17.3 per cent of 1,045 women under thirty-five, in 25.3 per cent of 1,235 women from thirty-five to seventy-five years, and in 28.6 per cent of 600 women between forty-five and seventy-five years.

The 42 patients gave the following as facts:

Maternal Grandmother: One died each of cancer of the stomach, and of the liver; in a third, the death cause was merely stated as "cancer."

Grandfather: One died of cancer of the stomach and one of the face.

Mother: Five died of cancer of the uterus, three of the breast, two of the ovary, two of the stomach, two of the bowel, and one from what was described only as "abdominal cancer."

Father: Two died of cancer of stomach, two cancer of the "neck," one cancer of the "face," one prostate cancer, one sarcoma of leg, and one cancer of "abdomen."

Aunt: One abdominal cancer, and two described only as death from "cancer."

Uncle: One cancer of the bladder.

Cousin: Cancer of the womb.

Sister: One cancer of the ovary, one each of breast, uterus, stomach, abdomen, and shoulder.

Brother: One cancer of the stomach, one of the tongue, and one of the jaw.

AGE

More than two-thirds of our 110 patients were between the ages of forty and sixty years, yet nearly all age groups were represented in the series. In general, the age curve of the ovarian cancers resembles that found in our 115 cancers of the uterine body. The average age of our women with ovarian cancer is greater than that of either our fibroid patients or those with cervical carcinoma, the age curves of which also resemble each other.

Two of our patients were less than nineteen years. One was a girl of sixteen who died with recurrence four months after removal of a very unusual type of

adenocarcinoma which developed in an ovary which also contained a dermoid cyst. The other patient was nineteen years of age, and had a large papillomatous cyst containing early carcinomatous change. Of interest also is cancer in old women. Ten of our series were between the ages of sixty-five and eighty-one. Five of these died of cancer within three months of their first treatment. One only lived more than nine months: oddly enough, this woman, aged eighty-one, was the oldest in the series, and lived for three and a half years: she had many "tappings." The curve showing distribution of age is shown as Fig. 1.

MENSTRUAL HISTORY

The time when menstruation began is within normal limits. Omitted from this calculation are the 6 granulosa cell tumor cases, and 12 other patients where data are not given.

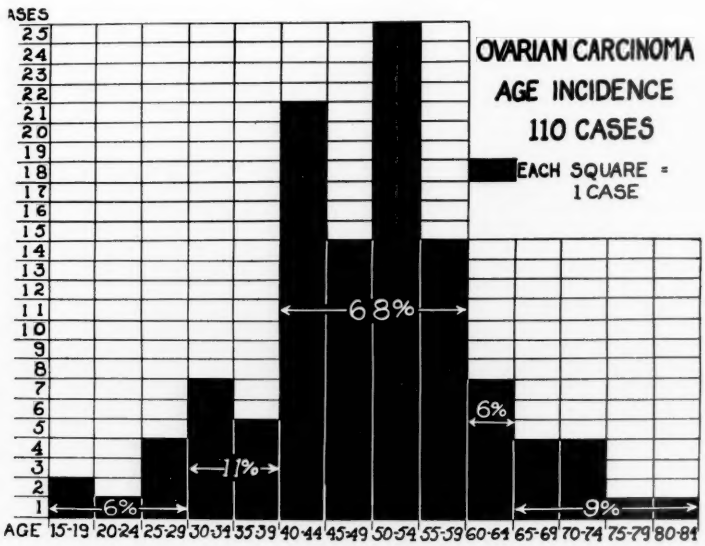

Fig. 1.

Nearly 30 per cent of the 92 patients did not begin to menstruate until fifteen years, or later, and nearly 10 per cent of them not until sixteen, or later. This is normal as is shown by a control study of nine groups, each of 100 gynecologic cases, in which menstruation first began at fifteen years, or later, in 22, 35, 24, 30, 30, 27, 35, 15, and 31 per cent respectively in each group. Another study of 300 women from which fibroids and menorrhagia cases were excluded showed that menstruation began at fifteen, or later, in 30, 30, and 27 per cent respectively in the three groups of 100 each.

TABLE I. ONSET OF MENSTRUATION

92 CASES—AVERAGE AGE 13.9 YEARS

YEARS	CASE	YEARS	CASE
10	1	14	26
11	4	15	13
12	13	16	15
13	18	17	2

When the patients presented for treatment, 40 already had passed through a normal menopause and had had no subsequent bleeding. Seventeen women were menstruating normally and regularly while eight were menstruating irregularly, scantily, or profusely. Two had amenorrhea at thirty-one years of age (one for four years and one for three months). Thirteen were having irregular periods and menopausal upsets, while 12 who had passed through the menopause some years before now had irregular bleeding. The six granulosa cell tumors were excluded also from this section of the compilation, as are twelve cases with incomplete histories.

MARRIAGE AND PREGNANCY

Nearly all series, especially in the older literature, contain a high percentage of unmarried women.

More recently, Byron and Berkoff found 23 per cent of ovarian carcinomas were in single women. Fleming had 20 per cent and McIntyre had 23 per cent in their series. Murphy's figure of 26 per cent more closely approaches the average found in the much older literature.

My own tables give a much lower percentage. Yet it is much greater than the incidence of unmarried women of comparable age in this country (U. S. Census 1920: 9.71 per cent of women over thirty-five years are unmarried; U. S. Census 1930: 9.26 per cent).

All authors report a high incidence of sterility in their series, yet often do not state whether the single women are excluded before the computation.

Cameron, in 1931, stated that 42.8 per cent of his 150 collected cases were nulliparas, and Szathmary, in 1935, found 35.2 per cent, neither author making comment as to whether any were single. Massabuan and Etienne, in 1913, excluded from their computation a number of girls whose ovarian cancers developed before puberty. Of those remaining, 97 had been pregnant, and 26 had not (27 per cent sterility). Strübler and Brandess, 1924, found that 28 per cent of 64 women, whose primary ovarian cancer had developed after the menopause, were sterile, whereas only one of 33 women who had secondary ovarian carcinoma had never been pregnant. Fleming (1931) reported 20 per cent sterility in the married of his series, and McIntyre, 1931, found sterility in 24 per cent of 78 married women with malignant and questionably malignant ovarian tumors. Murphy, 1935, gives sterility in 34.7 per cent of his series. Byron and Berkoff, 1926, found that ten of 44 married patients with ovarian carcinoma were sterile (22.7 per cent).

Strauss, approaching the subject from another angle, notes the small percentage of malignancy in ovarian tumors complicating pregnancy: the low point is one-half of 1 per cent (Siegel) and the high point is 6.6 per cent (Jetter) in such series. It is a fact, however, that the majority of pregnancies are in youth, and not in women of cancer age.

My own tables show a very high incidence of sterility in married women. Excluding the unmarried women from the calculations, I find that 31 per cent of patients had never been pregnant: and that 37.5 per cent had never borne a child—a few had had abortions.

Arranging the figures the other way, I find that only two-thirds of the married women had borne children, but that 42 per cent of the married women had aborted. These figures might challenge the assertion of Blair-Bell, and others, who claimed that parity was of no importance in the etiology of ovarian cancer, especially when we find that Hill, from data obtained from the U. S. Census of 1900, found that only 7.4 per cent of women in Rhode Island, Ohio, and Minnesota, married more than ten years had not been pregnant.

Data concerning abortion are unreliable because abortions often said to be spontaneous actually were induced.

Thirty-seven of my 93 married patients admitted from one to six abortions, 10 women acknowledging from three to six. Thirteen frankly stated that they had had from one to six induced abortions. Only 11 of the 37 women who had abortions subsequently bore a full-term child. Of these 11, 8 bore one child, and 3 bore two.

While too much importance cannot be ascribed to percentages obtained from a small series of cases, it is also true that the literature will never see a series of cancer observed within a single decade large enough to satisfy a statistician as to the accuracy of the deductions, and with sufficient social data to enable the reviewer at least to guess whether the relative sterility was caused by economic conditions, or inability to conceive.

The high incidence of abortion, and the few pregnancies thereafter, suggest that pelvic infection might be of etiologic importance. Yet pelvic infection is common in women of the childbearing age. If it were much of an etiologic factor for ovarian carcinoma, this tumor would be common, whereas it is rare. Two women in my series had ovarian tumors develop shortly after pelvic infection.

FIBROIDS

The rôle constituted by fibroids in sterility is not known. Whether fibroids are causal factors, or merely an occurrence in sterile women is still a question of contention. Nor do we know much more about their frequency in normal women.

We have few statistics on this point other than those of Cullen, who many years ago reported the finding at autopsy of fibroids in 10 per cent of 431 white women more than twenty years of age, and of Young and Williams, who found small fibroids recognizable only when the abdomen was opened at surgery in 2¾ per cent of 1,402 women. Fibroids were present in 20 of my 85 patients (all white) in which we were able to visualize the tumor. Most of them were small and of no clinical importance. Five other women had had operations for fibroids before our treatment. The incidence in the combined cases is 30 per cent. Three of the 20 fibroids might have been of clinical importance had their importance not been overshadowed by a malignant tumor.

FORMER OPERATIONS

Forty-nine of the 110 women had been operated upon several years before admission to my service, exclusive of several others who had had perineal repairs, curettage for incomplete abortions, operations for tonsils and adenoids, hemorrhoids and rectal fissures.

Thirty-five of the 49 had been operated upon many years before the patient could have had the cancer. Nine others had gynecologic operations so shortly before the patient gave evidence of cancer that I cannot be certain cancer was not then present. Five other women, however, were operated upon for stomach, gallbladder, or chronic appendix complaints when the cancer was present but unrecognized, although probably it was causing the symptoms. The fact that somewhere between 34 per cent and 40 per cent of the 110 patients with ovarian cancer had had the need of surgery in the past and unrelated to the present complaint merits attention, especially since I can find no such high incidence of former operative work in 330 gynecologic patients selected as controls. All of this latter group were more than forty years of age and none had tumors. They gave history of but 61 former operations, again excluding perineal repairs, curettage for incomplete abortions, tonsil, adenoid, nasal, and hemorrhoid operations, etc. This is an average of only 20 former operations in each series of 110 controls, the details being 11, 8, and 6 former general surgical operations in the patients with ovarian cancer, and 9, 17, and 10 former gynecologic operations in each group. The figures, however, do not show an unduly high relative proportion of former gynecologic operations, such as I found in patients with fibroid tumors, and which convinced me that a large number of women with fibroids had pelvic tissue that had always been below par. There were 16 former general surgical and 19 former gynecologic operations in the group of 110 ovarian carcinomas; 25 former general surgical and 36 former gynecologic operations in the 330 gynecologic patients over forty and without pelvic tumors, while there were only 71 former general surgical and 210 former gynecologic operations in 683 of my patients with fibroids.

SYMPTOMS AND SIGNS AND DIAGNOSIS

The fearfulness of ovarian cancer is shown by the fact that the disease so often developed insidiously. Sometimes the first symptoms were comparatively trivial, as a vague sense of pressure, or mild gastrointestinal upsets, and yet when the woman came for examination we found that she had an inoperable tumor.

The presence of a tumor was the first sign and only symptom in 6 cases. Two of these patients disregarded our advice and delayed operation until symptoms developed and compelled treatment. The other four did not delay treatment, yet all six had inoperable cancers when they came to surgery. Two only of these six women survived the five-year observation period, and both have recurrences. Dyspnea was the first symptom in several cases, caused by fluid in the chest in two, and abdominal ascites in several others. These also had inoperable tumors. It is startling to find the complacence with which so many of our patients regarded their enlarged abdomens. Some of them only felt that they were getting fat; a few, however, suspected fluid.

With patients coming in because of compelling symptoms, pain was the most common. Usually it was mild at first and not constant, and

then gradually increased in severity. When the pain was epigastric, there was often nausea and vomiting. A few patients came in with abdominal pain so severe that they were certain they had some acute abdominal condition. Sometimes the pain began in the ovarian region and radiated down the thigh, or to the groin or back. Yet the tumor was not always incarcerated in the pelvis when women had these symptoms. Pain, however, did not carry the meaning it does in cervical or uterine cancer, because many women who survived five years after treatment had pain as a symptom. We could not establish a definite relationship between pain and leucocytosis in a study of the cases.

Pain was a complaint in 40 of the 64 women who can be studied for five-year survivals. It was present for three months or less in one-third of the 40, between three and six months in another third, but was "felt off and on" in some form for several years before entry in the other third of cases. The sedimentation time was shortened invariably in the 20 cases in which it is recorded, sometimes being only twenty or thirty minutes.

The menstrual disturbances were variable. Twenty-five of our patients had postmenopausal or menopausal bleeding. When reviewed to see if the bleeding could have been due to fibroids, I find that only two of the 12 postmenopausal bleeding cases had small fibroids, as did two of the 13 women with menopausal bleeding. I did not think these tumors were the cause of the bleeding. Small fibroids were noted also in two women who had irregular menstruation, and in one who had amenorrhea of three months' standing.

Altogether, 316 complaints were given by 106 patients. Their incidence is shown as follows:

TABLE II. SYMPTOMS IN 106 OVARIAN CARCINOMA

Pain	In 70 patients	Bleeding	In 31 patients
Swelling	In 60 patients	Gastrointestinal	In 13 patients
Pressure	In 56 patients		In 6 patients
Tumor	In 39 patients	Amenorrhea	In 2 patients
Loss of weight	In 39 patients		

Physical examination did not always reveal the true character of the lesion when the growth was early, because then the findings were often only those of a pelvic tumor. Most of our errors were made when the woman had a small, fixed, unilateral tumor.

ERRORS IN DIAGNOSIS

The ovarian cancer was sometimes mistaken for fibroids when it was bilateral and the masses were indistinguishable from the uterus and there was no evidence of edema. It was erroneously considered cancer of the rectum in three cases that had rectal bleeding, ribbon stools, and mucous secretion. On the whole, however, the diagnoses

were remarkably correct, probably because there were so many advanced inoperable cases that came in with ascites and a frozen pelvis. One case, however, was missed completely: the patient had much ascites and a small ovarian tumor adherent to a freely movable mass that proved to be carcinomatous infiltration of the omentum.

Three of the six granulosa cell tumors were diagnosed as fibroids, an error easy to make but of no great importance with these tumors which, as a group, are usually relatively benign. None recurred after removal.

Thirteen ovarian adenocarcinomas were diagnosed as fibroids. Two only actually had them, together with an unrecognized ovarian cancer. One knew she had a "fibroid" tumor for seven years and had refused our proposed operation three years before and again upon entry.

We treated the four months' pregnancy size fibroid with radium and did not suspect the accompanying ovarian carcinoma until six months later when the mass was becoming larger instead of smaller. The other patient was treated by immediate operation and the fibroid uterus was removed together with the undiagnosed fist-size cancer. She lives twelve years after operation with a recurrence not yet very troublesome.

In 9 of the 11 remaining cases we erroneously diagnosed hard ovarian cancers as fibroids; 6 of these tumors were unilateral. In none was ascites present as a symptoms. Because operation, when conditions are proper, is the routine treatment of fibroids in my clinic, no harm resulted from the error save possibly in two patients. In one we diagnosed a symptomless "fibroid" and proposed operation which was refused. One year later, she returned saying she had had pain for several months. At that time there was no doubt but that she had an extensive cancer. The other woman was under the care of a competent physician for pain that could have no association with the pelvis. A small, hard, symptomless tumor was found on routine examination. The supposed fibroid grew rapidly within three months and caused symptoms. She then came to surgery and was found to have an inoperable cancer.

TREATMENT

Sixty-four patients were treated more than five years ago. Surgery was attempted in all, but in eight in whom there was abundant evidence that their condition was utterly hopeless. All of these died and came to autopsy. Two only of them, however, did not receive some form of ray therapy. The tumor was removed in 26 cases, nearly all with the uterus and opposite ovary as well. Twenty cases were operated incompletely: aiming to take as much tissue as possible with the hope that the roentgen ray therapy would be more effective if the cancer bulk was reduced in size. Ten operations were only exploratory, but afforded a chance of biopsy. Occasionally the tumor was tapped at operation to shrink its size and give better exposure for removal, but only when the case was absolutely inoperable—a spill from a cancerous cyst is never beneficial to the patient.

During the early years of the series, radium was used in 16 cases, sometimes followed by roentgen ray therapy. Four of these had radium preoperatively. In an-

other 4 cases, radium was placed within the tumor itself after a colpotomy. In 4 cases it was left for a short while in the pelvic cavity itself after an incomplete operation. In the other 4 patients, it was inserted into the uterine cavity after an incomplete operation.

Radon seeds frequently were inserted into metastatic nodules at time of operation. We no longer use radium, feeling that far better results can be obtained with the modern roentgen ray. The total dose of radium was never great. One patient received 5,770 mg. hours, the next largest dose was 4,200 mg. hours. I doubt if the radium treatments were of much value.

Roentgen ray therapy had been used almost routinely after operation since 1919, and frequently before it. Until 1925, the machines ran between 120 and 140 K.V. The treatment, however, was usually

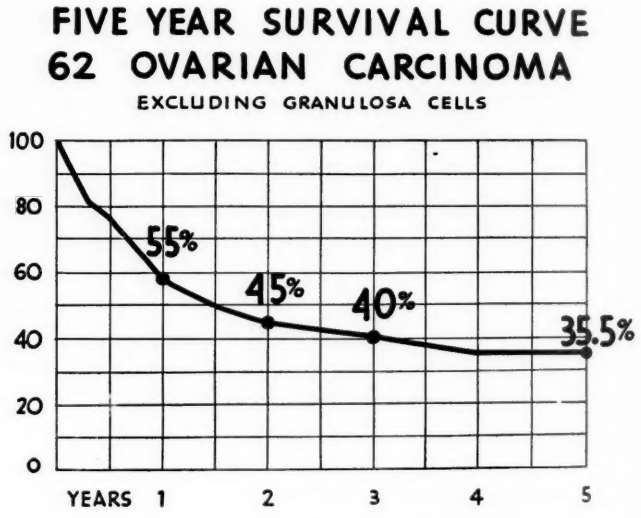

Fig. 2.

incomplete, often being cut short because of x-ray sickness. From 1925 to 1929, nearly all of the patients were treated with 160 K.V. machines, but since 1929, 200 K.V. machines have been used. During these years, ideas concerning roentgen ray treatment have suffered radical changes. Screenage, portals of entry, and the size of the field have been changed almost year by year. X-ray sickness, however, still continues. Only since 1929 has roentgen ray therapy been given in a manner at all comparable to that in which it has been used the past three years.

CURES

By common usage, but not correctly, our 64 cases could be considered for percentages of five-year cures. Yet, we have excluded the two granulosa cell tumors from the computation, because we are primarily

interested in the more malignant ovarian cancers. Properly speaking, five-year cures mean freedom from evidence of recurrence five years after the last treatment, but most of our patients have been radiated several times since then, or even reoperated upon once or twice. Reports in the future, however, will not have this objection. Most of us have learned the dangers of reradiating a patient who has had a full course of treatment with a modern machine. With our large machine, running with one million volts, and the rays screened with 2 mm. of lead, 1 mm. of copper, and 1.5 mm. of aluminum; and the patient's body 17 cm. thick, my colleague, Dr. Robert Stone, has found that 18 per cent of the rays pass completely through a woman's body.

Under the above definition, we have 22 of the 62 patients alive at the end of five years after our first treatment, 35.5 per cent so-called five-year cures. By proper standards, the five-year cures are restricted to patients without evident recurrence five years after the last cancer therapy. Here we have only 11.8 per cent of cases, 11 papillary cystomas with malignant areas, one pseudomucinous adenocarcinoma, and two primary adenocarcinoma. Roentgen therapy supplemented operation in only four of these patients, and radium in four; for details see Tables I, II, and III.

COMMENT

A five-year cure rate of 35 per cent (37 per cent if the granulosa cell cancers are included) seems very gratifying on first sight. Careful scrutiny of my work sheets dispels this thought. First, because many patients have been reoperated or reradiated during a period in which they should not be re-treated but merely observed. Also because some of the slow growing tumors that had been re-treated might have been still present but unrecognized on examination after five years: yet later they might develop and cause death. Second, the cure rate depends largely upon the number of slow growing tumors in the series, important because years may pass before their metastases attack vital organs. For these reasons it is useless to attempt the evaluation of any method of treating ovarian cancer unless the patient has been followed for a minimum of ten years from the date of the last treatment. There are no reports as yet in the literature based on such thought.

We cannot expect to cure the majority of ovarian cancers because the great proportion are inoperable long before they cause symptoms which send them to a physician. "Inoperable" still means what it did before x-ray and radium came into the therapeutic field and when surgery alone offered chance of cure. "Inoperable" then and now means practically incurable even though radium and x-ray have accomplished wonders in a palliative way. Yet inoperable cancers do not invariably kill within five years, no matter what treatment or none has been employed. Numerous reported cases attest this fact. Quite

TABLE I. PAPILLARY CYSTOMA WITH CARCINOMATOUS CHANGE

SURVIVAL YEARS	TUMOR	OPERABLE	REOPERATED	REMOVAL	CYST BROKEN	FLUID	RADIUM	ROENTGEN RAY	FORMER PELVIC OPERATION
				Patients Living—Pelvis Free					
18	Single	Yes	No	Complete	No	No	2600 mg. hr.	No	No
17	Single	No	No	Incomplete	Yes	No	No	Yes	No
17	Double	Yes	Yes	Complete	Yes	No	2800 mg. hr.	No	No
13	Double	Yes	No	Complete: cut ureter	Yes	Yes	No	Yes, after 9 months for recurrence	Colpotomy for pus tubes, three years before
12	Double	Yes	No	Complete	Yes	Yes	No	Yes	No
10	Single	Yes	No	Complete	No	Yes	No	No	No
9	Double	Yes	No	Complete	No	No	No	Yes	No
6	Double	Yes	No	Complete	No	No	No	No	No
				Died—Suicide: Pelvis Free					
6	Double	Expl. only and 600 mg. hr. radium in tumor	3 years later; BSO supravag. hyster.	Complete 2nd time	No	Yes, first time	600 mg. hr.	No	No

				Died—Carcinoma					
8	Single	No	No	Incomplete	Yes	No	No	Two courses	Question of ovarian cancer before, with no path. report. Ovary out 2 yr. before. Also "pelvic tumor." Some fluid.
6	Single	No	Yes: tumor 3 yr. later; expl. 4 yr. later	Incomplete	Before operation	Yes	5770 mg. hr.	Much	Ovarian tumor, possibly cancer, two yr. before. Also x-ray.
7	Double	Yes	No	Complete	No	No	2000 mg. hr. 6 yr. later, 1 year before death.	No	No
				Living—With Carcinoma					
13	Single	Yes	No	Complete	At oper.	No	No	No	No
12	Double	No	No	Of primary tumor. Metast. cauter. Omentum resected	No	No	No	Yes	No

recently Coffey and Humber reported 108 survivors among 991 patients whose cancer (various organs) was adjudged inoperable and hopeless when first seen by them. Only in operable cases may we confidently expect permanent cures, and truly operable cases form a pitiably small percentage of the total series. Operable cases, moreover, can be expected only when the tumor is slow growing and of low malignancy. My series emphasizes this view.

My 22 five-year survivors, some of whom presumably still had nonpalpable cancer, comprised 14 women with cancerous areas developing in otherwise benign papillary cystomas, 3 with pseudomucinous tumors and 5 with primary adenocarcinomas.

The 14 papillary cystomas are relict of the 18 such cases of the total series. In all instances the tumor was essentially macroscopically benign although cancer was proved to have been present. The diagnosis, therefore, was microscopic rather than macroscopic, yet 4 of the 18 patients died from cancer before the expiration of the five-year observation period. The 14 survivors fall in four groups. The first consists of 8 women who are living and well and apparently cancer-free. The second consists of one woman, suicide when well for six years. The third consists of 3 patients dead of cancer after the expiration of the five-year observation period, dying six, seven, and eight years respectively after first treated by me. The fourth consists of 2 living with cancer, thirteen and twelve years respectively after my treatment.

In considering the first group, the reader will note from Table I that the cyst was broken at time of operation in 4 of the 8 women who are cited as apparently well and cancer-free. Three of the 4 had roentgen ray therapy. The tumors were removed completely and unbroken in the other 4, only 1 of whom also had treatment with x-ray.

The rôle of roentgen ray therapy in the treatment of these cases merits discussion. Theoretically, papillary cystomas do not react favorably to the rays since the connective tissue cords are surmounted by a single layer of epithelium. Yet the x-ray must have been the curative factor in 2 patients, 1 who survives an incomplete operation after seventeen years; and another who nine months after surgery developed a recurrence that disappeared after radiation, and has not reappeared after thirteen years. Its effect cannot be evaluated in the third patient because the fourth patient also with a cyst ruptured during the removal of the tumor had no roentgen ray and yet survives seventeen years cancer-free. The cure cannot be well ascribed to 2,800 mg. hr. of radium which was given in the vaginal vault after the first operation. A subsequent operation removed a fist-size mass of papillomatous materal, none of which has recurred. Surgery for a tumor of low malignancy may properly be credited with the cure.

Roentgen ray therapy cannot be considered of marked curative value in one case in which it was used after the complete removal of the pelvic organs, the patient now living nine years, because two similar tumor patients were treated only by the surgery and lived ten and six years, respectively. The fourth patient in whom the tumor was completely removed unbroken also had 2,600 mg. of radium through a colpotomy wound. It is difficult to conceive that the survival of eighteen years is due to radium rather than the complete removal of a tumor of low malignancy.

The one patient who died from suicide six years after my first treatment is very difficult to understand, because her first operation was exploratory—the cancer did not seem to be one that could be removed completely. Six hundred millicurie hours of radium consequently was given in the body of the tumor through a colpotomy wound. Three years later the tumor was not larger but the woman complained bitterly of vaginal discharge and the fistula. Consequently, I reoperated upon the patient and found to my astonishment that I could remove the tumor practically complete. The growth had not returned three years later (when she died), although the patient had never had roentgen ray. Whether this tumor shrank spontaneously in size cannot be determined. I am certain it was inoperable when first seen. It does not seem likely that 600 mc. hr. of radium could act in such a wonderful manner.

The three women who died of cancer subsequent to the five-year follow-up are of much interest. Two of them may have been survivals due to the slow growing tumors and the surgery rather than to the x-ray. One dead eight years after our surgery may well have had a cancer of the ovary removed two years before admission here, the physician reporting a large ovarian tumor and much fluid as her pathology at that time. The cyst was broken at our operation, consequently was incompletely removed. Subsequently she had several courses of x-ray. The second patient of this group died six years following our surgery, also worthy of note since she also had an ovarian tumor removed and x-ray treatment given two years before her entry here. She was reoperated and again reoperated after my first surgery and each time cancerous material was removed. In the meantime, she had two other courses of x-ray and 5,770 mg. hr. of radium given in the vaginal fornices and culdesac. The third patient was free from recurrence for six years following radical surgery, when the tumor returned and did not react to radium through the vaginal fornix. The fact that papillary cystoma may grow very slowly seems proved by one other patient living thirteen years after operation but with a slow growing metastasis. The cyst was broken during my attempt to remove it, but seemed completely removed. She has received neither radium nor x-ray.

Many urge that roentgen rays cause the disappearance of peritoneal metastases after the primary tumor has been removed fairly completely by surgery. It may so be. Yet it is equally likely that the implants from a cancer of low malignancy disappear spontaneously after the ovary has been removed and its internal secretions stopped. Such phenomena occur in endometriosis after the ovaries have been removed or killed by x-ray. Small metastases on the bladder, or the peritoneal wall of the sigmoid occurred in several surviving cases with papillary cystoma and were treated with the cautery. Until recent years, I ascribed the cure of the metastases to the cauterization of these nodules. Now, however, I feel that they disappeared spontaneously after the removal of the primary tumor. One patient surviving twelve years, but now living with cancer, had such metastases and omental involvement. The omentum was resected. She also had x-ray.

The 3 pseudomucinous tumors also merit attention since in only one was carcinoma noted at the time the primary tumors were removed. The patient survives nine years without evidence of recurrence; she had had neither radium nor x-ray. The 2 other pseudomucinous patients died from cancer thirteen and eleven years respectively after our first operation. The tumors in both cases ruptured before my first operation and pseudomucinous peritonitis followed, necessitating re-operation once repeated again. Cancer presumably appeared a year or two before death and was proved at autopsy. Both women had received much x-ray therapy during their last years without apparent benefit (Table II).

Five of the 39 women with tumors I adjudged to have been carcinomatous from the beginning survived for five years. These more cellular tumors should be more favorable for treatment with the roentgen rays. There is no doubt that the x-ray was responsible for prolonging life in 2 of the 5 cases and possibly a third. In 1 of the 2, the operation was only exploratory since the tumor could not be removed. She had much x-ray in the years that followed, and six years later when the tumor had not increased in size, we explored again. The tumor mass then was not larger, but was still inoperable and the entire abdomen now was fairly studded with metastases. She lived seven years after my first exploratory operation. The second woman had an incomplete operation followed by x-ray. The tumor returned four years later and is still present, although held in check by another full course of the roentgen rays. She lives seven years. X-ray may have been helpful for one patient now living and well for six years. Her cyst was broken when she came to operation: she had much fluid and many metastases in the lower pelvis which I treated with a cautery. I doubt if she will prove a permanent cure. On the other hand, the 2 patients who survived the longest (one fourteen

TABLE II. PSEUDOMUCINOUS CYSTADENOCARCINOMA

SURVIVAL YEARS	TUMOR	OPERABLE	REOPERATED	REMOVAL	CYST BROKEN	FLUID	RADIUM	ROENTGEN RAY	FORMER PELVIC OPERATION
Patients Living—Pelvis Free									
9	Single	Yes	No	Complete	No	No	No	No	No
Died—Carcinoma									
13	Double	No	Yes, twice	No	Before op.	Yes	No	Much	No
11	Double	No	Yes, twice	No	Before op.	Yes	No	Yes	No

TABLE III. PRIMARY CARCINOMAS

SURVIVAL YEARS	TUMOR	OPERABLE	REOPERATED	REMOVAL	CYST BROKEN	FLUID	RADIUM	ROENTGEN RAY	FORMER PELVIC OPERATION
Patients Living—Pelvis Free									
6	Double	No	No	Primary tumors; metast. cauter.	Before	Yes	No	Yes	No
Died, Heart—Pelvis Free									
14	Single	Yes	No	Complete	Yes	No	1327 mg. hr.	No	No
Living—With Carcinoma									
7	Double	No	No	Had metastases	Before	Yes	No	Two times	Ovary resected. Tube and fibroid out 15 yr. before.
Died—Carcinoma									
13	Single	Yes	No	Complete	Yes	No	1160 mg. hr.	No	Vag. hyst. fibroids; one ovary out 6 years before.
7	Double	No; expl. only	Yes; expl.	No	Before	Yes	No	Much	No

years, dying cancer-free from heart disease, and one thirteen years, dying from a recurrence) received no roentgen ray. Small doses of radium, however, were given in both cases, the former 600 mg. hours, and the second 1,160 mc. hr. in the culdesac after the primary tumors were removed. The cases are worth citing at some length.

One woman, who had had a vaginal hysterectomy at forty-four, began to lose weight and strength at fifty years, four months before entry. She had complained of dragging pain on the right side of the abdomen, and groin, intermittently for three months, then almost constantly, keeping her awake at night. It did not change character or position, nor was it modified by meals or the condition of the bowels. The lower abdomen became enlarged a few weeks before entry, whereas it had been flat before. At operation, I found an ovarian cancer 12 cm. in diameter fixed in the pelvis and lower abdomen. It ruptured during removal with discharge of some serous material; some visible particles of the mass could not be removed, and were left on the lateral pelvic wall. Because the operation was not complete, I placed radium in the culdesac and drained through the vagina. The radium dose was only 1,160 mg. hours. The microscopic findings showed a rather wild looking medullary carcinoma which contained cavities filled with hemorrhage and necrotic débris. I felt her condition was hopeless, and as she was not strong enough to stand roentgen ray therapy, I sent her home. From time to time, she wrote me that she was perfectly well, and her abdomen was flat again. Her physician frequently reported negative findings. Twelve and one-half years after this treatment, she returned with a bowel obstruction which caused death. At autopsy, the abdomen was full of cancer of the same type as the primary tumor. Had this woman received roentgen ray therapy after operation, I would have counted her as a five- and even ten-year cure, due entirely to roentgen ray.

The other patient had an enlarged abdomen and pain for three months as a symptom and a unilateral disgerminoma which completely filled her pelvis and was firmly attached by its unbroken capsule to the pelvic wall. The cyst was broken during removal, yet I suppose was rather completely removed. I left 100 mg. of radium in the culdesac for fourteen hours, having made a colpotomy wound. She was desperately sick after the surgery, far too sick to receive roentgen ray. She went home to die, yet returned two years later, practically well. She died fourteen years later from a cardiac lesion without ever giving sign or symptoms that she had ever had a cancer. This case also must be regarded as a cure by fairly radical surgery of a cancer of comparatively low malignancy. Had she had roentgen ray therapy at any time following surgery, I would unhesitatingly credit the cure to the roentgen ray (Table III).

The above review convinces me most firmly that the profession erroneously credits too many cures of ovarian cancer to the roentgen ray. The agent has proved most helpful in a considerable number of advanced cases where the growth rapidly shrank in size and fluid was markedly decreased. Yet at least as many cancers did not respond at all. Moreover, if a patient remains well five or more years after the complete removal of the tumor and subsequent roentgen ray, the important factor in the apparent cure is not as likely to be the radiation as many observers claim. More likely is it to be the complete removal of a cancer of low malignancy. By no means would I restrict the use of the therapeutic roentgen ray as adjuvant to surgery. We should always use it but keep an open mind concerning our results. We will learn facts more certainly and much faster if we follow all our cases through their entire period of survival after our treatment

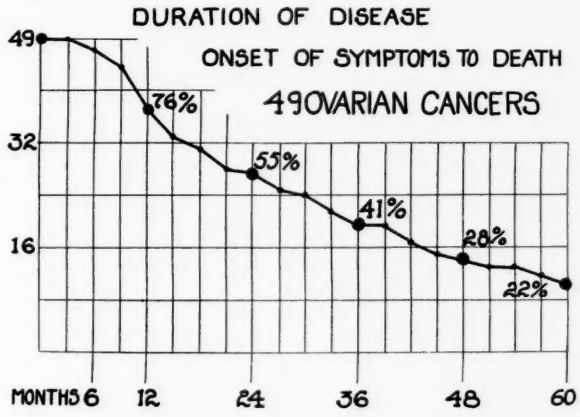

Fig. 3.

before we attempt to evaluate the factors responsible for cure. Only by so doing can we learn the laws that govern the growth of these cancers that now are an unknown factor in determining the frequency of so-called five-year cures.

Tables I, II, and III give the essential data concerning my five-year survivors.

Figures showing the duration of the disease from the onset of symptoms to death in the 49 nonsurvivors show many more slow growing than rapidly growing tumors in my series. Careful study of the microscopic sections gave no support to the theory that the histologic grading of the epithelial cells was of value in determining the radiosensitivity of the tumor and the prognosis for the patient. The entire known course of the disease after symptoms was less than six months in 2 patients; between nine to twelve months in 9 (24 per cent dead within the first year); between one and two years in 10 (21 per cent),

two and three years in 8 (14 per cent), between three and four years in 6 (13 per cent), between four and five years in 3 (6 per cent). The 11 who were alive five years after the beginning of symptoms (22 per cent) died at various periods, two of them as late as fourteen years after their first symptoms. Most patients surviving five years had intervals free from symptoms when I considered them cured. Two patients now are living but with evident cancer fourteen and thirteen years respectively after their first symptoms. Their cancer has not yet attacked vital structures. The curve as a whole bears a striking resemblance to that of the five-year survivors.

CONCLUSIONS

1. Two-thirds of 110 ovarian carcinomas occurred in women between forty and sixty years of age.

2. Forty per cent of the patients gave a history of cancer in other members of the family.

3. Twelve per cent of the patients had never married.

4. Thirty-one per cent of the married women had never been pregnant.

5. Five-year cures were obtained only when the malignant areas were encapsulated by a cyst wall, or when the tumor was of low malignancy.

6. The value of present therapy cannot be determined with a follow-up of less than ten years' duration, during which period the patient should not be re-treated but should only be observed.

7. The curative effect of roentgen ray therapy in ovarian tumors is much overstated.

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DISCUSSION

DR. DEWITT B. CASLER, BALTIMORE, MD.—Ovarian cancer is insidious in its onset, coming in most cases at a time when women are least conscious of their pelvic condition, beginning usually without bleeding, with pain as the most essential symptom, and inoperable from the time when first seen by the surgeon. The five-year results in ovarian carcinoma are therefore about the poorest of any of our surgical procedures.

The family history of cancer in this series is most interesting to me, 40 per cent having had a positive history in their families. Many of these patients appear to

have a distinct susceptibility to malignancy as I have had three cases of adenocarcinoma of the ovary in which the patient had carcinoma elsewhere. Two cases of adenocarcinoma had also a carcinoma of the breast, and one an associated carcinoma of the sigmoid.

I have long been under the impression that there was a marked disparity in the occurrence of malignant cystadenomas in the white and black races. The last 50 or 60 cases in the Johns Hopkins laboratory showed that the frequency in the whites over the blacks was about 5 to 1. In the granulosa-cell tumors the incidence was about the same for the two races.

It might be interesting to report a Krukenberg tumor that came to me a few years ago. This patient had been operated upon nine months previously for an ulcer of the stomach. Under microscopic examination the ulcer showed a few very peculiar cells which, however, could not be termed definitely malignant. Nine months later this patient came under my observation, and I found Krukenberg tumors of both ovaries and very well-marked carcinoma of the stomach. This gives us a picture of the rapidity of the life history of these tumors.

The results of radium and x-ray treatment of the spindle cell sarcoma are not very satisfactory. In one case where the tumor could be removed except for a very small area in the culdesac, where radium could be placed almost directly on the growth, I assured the family that x-ray should do a great deal but after treatment the tumor spread rapidly. On the other hand, I have just seen a patient who had exactly the same type of spindle cell cystic ovarian tumor, who was operated upon ten years ago and the growth was incompletely removed. That patient has had no x-ray or radium treatment and she is still alive, although she came the other day for a paracentesis.

As far as the treatment of these various ovarian carcinomas are concerned, there seems to be very little difference of opinion about the operative treatment. Since ovarian malignancy is so often bilateral and because it often spreads to the fundus of the uterus, it is generally agreed that complete removal of the pelvic organs and as much of the tumor growth as possible should be done. We have found that most malignant tumors of the ovary respond to x-ray and radium, although the papillomatous cystic carcinomas do not respond so well as the solid, massive type.

There are times when the increase of the growth is restricted in a remarkable way. A colored patient was operated upon by Dr. Cullen six years ago for a very extensive carcinoma of the cystic type which he was unable to remove. No treatment was given after operation because he thought it would not be of help. The patient was readmitted during the next six years 52 times and a total of over 1,000 liters of fluid removed before she finally died of a kidney infection. Autopsy revealed not only a general carcinosis but a generalized tuberculosis of long standing. The pathologists have been extremely interested because in many areas of the abdomen the tuberculous process had strangulated the carcinoma and stopped the growth.

DR. ROBERT A. KIMBROUGH, PHILADELPHIA, PA.—I have briefly summarized a group of 89 cases of ovarian carcinoma from the records of the University of Pennsylvania Hospital.

We have found that histologic grading of these cases is of little or no value in prognosis, and, consequently, we depend entirely upon the gross extent of the disease in predicting the chance of cure.

Group I is comprised of cases in which the whole malignant process was apparently confined to one or both ovaries; 37 per cent of our cases fell into this group. In 38 per cent the primary growth could be removed although some peritoneal implants were left behind (Group II). In the remaining 25 per cent removal of the primary growth was impossible because of widespread metastases (Group III).

The five-year salvage in these groups is as follows: Group I, 85 per cent; Group II, 21 per cent; Group III, 13 per cent. It was interesting to note that 90 per cent of the fatalities occurred within two years following operation.

The value of postoperative x-ray treatment is well exemplified by a small series of cases in which the primary growth was removed but peritoneal metastases were left behind. Five-year salvage was obtained in 43 per cent of this group following postoperative irradiation, while only 13 per cent survived among those who received no x-ray treatment.

DR. WILLIAM P. HEALY, NEW YORK, N. Y.—An important point in the handling of ovarian tumors is that we must not be discouraged by the presence of a large amount of free fluid in the peritoneum or even in the chest cavity. We have had such cases sent to us as incurable but with the removal of the fluid it could be demonstrated that the patient had only bilateral ovarian fibromas.

As to the question of histology and its relation to prognosis, it is interesting that we have had four young women with the embryonal histologic type of cancer of the ovary where a competent surgeon has removed the original tumor and left the other ovary. Usually within a year another large tumor had appeared in the other ovary and the patient was referred for radiation, being considered inoperable. In each instance the tumors have disappeared in from six to eight weeks after irradiation, and the patients have remained well for from six to nine years.

A similar striking case was that of a young woman nineteen years of age, practically carried into the clinic three years ago, with a story of having had a cesarean section a year and a half previously with the removal of a malignant ovarian tumor. She came to the Memorial Hospital frightfully ill, with a large abdomen and multiple tumor masses. The original surgeon reported that the growth had been a very anaplastic type of ovarian cancer. After two months of roentgen therapy we could not find any tumor except deep in the pelvis, and that eventually completely disappeared.

Preoperative roentgen radiation for ovarian cancer is the secret to whatever success you will attain. I have never seen the primary tumor of a papillary adenocarcinoma of the ovary disappear under radiation therapy, but the secondary implants are extremely radiosensitive. In one patient operated upon and regarded as incurable, then treated for two years by tapping and roentgen irradiation at intervals, I have been able ultimately to remove the primary tumor. It is now eight and a half years since I did this in one case.

The worst results are obtained in the patients already operated upon by surgeons who have torn widely into the tumor tissue, opened up lymphatic and blood spaces, but have left a lot of residual cancer. We can only help these patients for a little while with postoperative radiation. I am now teaching that if we believe that a patient probably has a malignant ovarian tumor, and she is beyond the age of forty, radiation treatment should be given and then a delay for several months before operating.

The importance of preoperative radiation is seen in another case. This patient had had amenorrhea for three or four months, and had an enlarged abdomen with palpable tumor masses. Preliminary roentgen irradiation was advised and the abdomen tapped once. No more fluid formed, and six months after coming under my observation we were able to remove the tumor masses and the uterus. There was no evidence of secondaries elsewhere and no more tumor has since formed.

The case with the longest history of tapping that I have ever seen any reference to, was a patient coming with the story of a failure to remove an ovarian tumor seventeen years before and repeated paracentesis ever since. She was a huge woman and when she came to the Memorial Hospital we advised roentgen radiation. Later in spite of the seventeen years of constant tapping we were able to remove all of the tumor tissue. This shows the tremendous resistance of the peritoneum to infection.

DR. CHARLES C. NORRIS, PHILADELPHIA, PA.—I believe ovarian tumors vary markedly in radiosensitivity. I have seen many cases which were extremely radioresistant. I should like briefly to relate the history of a case which was in some ways extremely susceptible to deep roentgen therapy. This patient, a woman suffering from papillary adenocarcinoma of both ovaries, was operated upon by the late Dr. John G. Clark, a complete operation being performed. No post- or preoperative irradiation was given. Eighteen months later she was brought to the hospital in an ambulance suffering from a recurrence. The pelvis was "frozen" and in the abdomen a firm, fixed mass rose to two fingerbreadths above the umbilicus. There was considerable ascites and there had been a loss of 20 pounds in weight. The patient had been absolutely bedridden for two weeks. Deep roentgen therapy was instituted and in three months the mass had been reduced to an oval fibrous lesion in the left wall of the pelvis about the size of a pigeon's egg. At six months after the irradiation this mass had increased to the size of an orange or small grapefruit and a small amount of ascites was demonstrable, a second course of deep roentgen therapy again reduced the recurrence to a pigeon's egg in size. During the next six years there were 4 to 5 similar recurrences, each one treated in the same way and with the same result. Histologically the original specimen presented the usual characteristics of a papillary adenocarcinoma. The case is of interest for the following reasons: (a) the speed with which all the recurrences yielded to roentgen therapy; (b) the fact that although the tumor was evidently highly radiosensitive a cure was not effected despite the many courses of deep roentgen therapy administered; and (c) the fact that no immunity to the rays was developed, the last recurrence yielding as quickly as the first. This patient finally died of a strangulated hernia while out of the city and about seven months after the last recurrence. The case is not recorded as a cure and, as it occurred twenty years ago, did not have the advantage of more recently developed methods of irradiation.

In our series of cases previously reported from the University of Pennsylvania Hospital, we found that the papillary adenocarcinoma (not simple papilloma) yielded about 50 per cent better five-year salvage than the glandular carcinoma and that the secondary carcinomas (i.e. those developing in previously benign neoplasms) gave about twice as good end-results as were secured from those which were malignant from the onset.

We have not found the microscope of great aid in determining radiosensitivity in ovarian tumors. The large variety of malignant neoplasms which develop in this organ greatly hamper careful end-result study. In our study, simple papillomas were classed as semimalignant and were therefore not included in our series.

DR. EMIL NOVAK, BALTIMORE, MD.—It would be valuable if we could discuss separately the end-results of the various types of ovarian cancer. Unfortunately, Dr. Lynch's pessimism is fully justified with most forms of ovarian carcinoma. With others the outlook for the patient is not nearly so bad. This would apply, for example, to many cases of granulosa cell carcinoma, but not to all. A large number of cases of this type have been cured by nonradical operations, such as unilateral salpingo-oophorectomy. On the other hand, we have had cases in our series of over 50 in which even after very radical operations the tumor has returned with amazing rapidity. In one patient, for example, within three months of a very complete operation, the patient returned with a recurrent tumor filling the pelvis and soon proceeded to a fatal termination. Metastases to the long bones have been observed in a few cases in the literature.

On the other hand, the Brenner tumors, while usually classed with the carcinomas, seem to be essentially benign, and I know of only one case in which recurrence is said to have been noted. The disgerminoma or seminoma, again, is apparently much less malignant than ovarian cancer in general, and in addition is quite radiosensitive.

Krukenberg tumors, being almost always, and according to many always, secondary, offer very little hope to the patient. Although not especially germane to the present discussion, I believe there is good evidence that the Krukenberg tumor may in rare cases be primary in the ovary, and I have observed one or two cases in which this seems to have been the case.

In short, there is no field of clinical gynecology in which pathology is so essential to the proper interpretation of findings and results, and no field of gynecologic pathology which is in greater need of clarification than that of ovarian tumors.

DR. FRED L. ADAIR, CHICAGO, ILL.—We have had the greatest difficulty in knowing what we might expect from either irradiation or operation, and in many cases where we had expected good results we had disastrous ones, and vice versa.

With reference to the particular group of papillary cystomas, we have great difficulty in determining whether these tumors are really malignant. It is obvious that we cannot examine the whole tumor microscopically, and in isolated fields we have difficulty in determining whether a particular field is definitely malignant or not. So I believe we have to accept with more or less skepticism the diagnosis of malignancy in the enormous tumors of this type owing to the impossibility of making a microscopic examination of all portions of the tumor.

One point which must be stressed, in view of the possibilities of irradiation treatment, is the examination of the cellular elements in the fluid, obtained by a paracentesis. It is often possible to make the diagnosis in this way without any exploratory operation. Heretofore we have favored exploratory operation prior to irradiation, but if Healy's opinion is correct, we believe paracentesis for diagnosis with subsequent irradiation and ultimate operation would be preferable.

DR. J. C. LITZENBERG, MINNEAPOLIS, MINN.—We recently analyzed our cases of cancer of the ovary at the Cancer Institute of the University of Minnesota, and our results were so good that I hesitated to report them. But inasmuch as our figures closely parallel those of Dr. Lynch, I have the temerity to say a few words about them. Of our 108 cases nearly 33 per cent were well five years afterward, some of them nine years. This year will have to be completed before we finish the ten-year period.

I also have been impressed with the unreliability of the pathologic diagnosis because of the inherent difficulty of making a satisfactory examination. As an illustration, in one patient the entire peritoneal cavity and intestines were studded with implants that microscopically were diagnosed as cancer. For mechanical reasons the tumor was removed in spite of the apparently hopeless prognosis, and she did not have x-ray treatments. That was eight years ago and she is well at the present time. Five years afterward it was necessary to open the abdomen for another gynecologic condition, and there were none of those implants left. They could not have been malignant, the only treatment having been removal of the cyst.

Our method of treating cancer of the ovary is to remove the cyst and follow our surgery with deep x-ray therapy. Perhaps Dr. Healy's method of preoperative roentgen therapy may be better, but inasmuch as our results are almost parallel with Dr. Lynch's, I thought our figures might be reported here in spite of the fact that we feel that they should be rechecked before publication.

We agree with Dr. Lynch that we should studiously avoid the term five-year cure. We only say five years alive and without recurrence. After ten years perhaps we can say something more definite and reliable about the cases.

DR. LYNCH (closing).—My study has convinced me that x-ray is not the curative agent with ovarian cancers that we have thought it to be. Occasionally it does wonderful things as Healy has described. It sometimes controls fluids but very,

very often fails. When you follow your patients for many years you will come to believe with me that the tumor that is x-ray sensitive is likely to recur. Lymphosarcomas are most sensitive to x-ray, yet x-ray has never cured one of them.

It so happens that we have many patients in our series who were treated with such small doses of radium that the cure must be credited to surgery even though we felt the removal was not perfect. Especially is this true of papillary cystomas, the removal of which is likely to cause recession of peritoneal implants. Papillary cystomas are not sensitive to x-ray yet this is the group of tumors in which we have had the greatest percentage of cures. The tumors which were essentially epithelial are the ones which x-ray should cure, but our results do not force such a conclusion. Possibly these tumors were too widespread, yet several early cases did not react to radium and several others did not recur after complete removal. In the treatment of ovarian carcinoma as in any other malignancy we must be careful in deciding whether the cure was because of the treatment or just happened to follow it. Only by carrying your cases for ten to fifteen years will you know anything as to what your results have been in this blind type of cancer.

ILIAC LYMPHADENECTOMY PLUS RADIATION IN BORDERLINE CANCER OF THE CERVIX*

FRED J. TAUSSIG, M.D., ST. LOUIS, MO.

(From the Gynecologic Service, Barnard Free Skin and Cancer Hospital, St. Louis)

TWO years ago I described a method of treatment for borderline (Group II) cancer of the cervix, combining radiation of the primary lesion with surgical removal of a large portion of the tributary lymph glands. The first case done in October, 1930, with cancer metastasis in the hypogastric lymph glands is still free of recurrence at the present time, five and one-half years later. In this first report† I separated the cases into Group II and Group III (League of Nations Classification). The patients in Group III had so high a primary mortality that I have not done the operation in these more advanced lesions during the past two years. The total number of patients in Group II operated upon up to the present time is 46.

The experience of the past two years has encouraged me in the belief that by this method of treating borderline cancer of the cervix we have made some little advance, and, Heaven knows, when we are attacking so formidable an enemy as cancer, even a gain of 10 or 15 per cent seems like a victory.

Victor Bonney in his discussion last year agreed to the general principles of this method, even though he could give no definite figures as to the number or results in the cases where he had removed

*Read at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25, 1936.

†Iliac Lymphadenectomy with Irradiation in the Treatment of Cancer of the Cervix, Am. J. Obst. & Gynec. 28: 650, 1934.

lymph glands alone. It was also of great interest in this connection that 23 per cent of Bonney's patients who had cancer metastasis in lymph glands remained well over five years.

SELECTION OF CASES

Careful selection of cases is a prime requisite to success. First and foremost the patient must be a good operative risk. Heart and kidney disease, obesity, debility or extreme age are contraindications. Just because cancer has a greater tendency to early metastasis in the young, I have applied this method wherever possible to younger individuals. The average age of the 46 patients subjected to lymphadenectomy was forty-one years, compared to forty-six and one-half years for the entire group of cervical cancer patients treated during this period of time. Fifteen patients were thirty-five years of age or less, and five were between twenty-two and twenty-nine years of age.

MORTALITY

There have been two deaths among the 46 patients operated upon up to the present time, a primary mortality of 4.3 per cent. An analysis of these two deaths shows that the concomitant radiation was an important, if not the main, cause of the fatality. One patient died eight days after operation of embolism probably due to a gold radon seed implanted close to the uterine vessels. The second death occurred on the sixth day after operation from peritonitis. At autopsy it was shown that the radium capsule placed in the cavity of a bicornuate uterus, whose rudimentary horn had been removed, caused a slough and perforation into the broad ligament, with infection spreading thence to the abdominal cavity. These two deaths have induced me to avoid all radiation treatment at the time of operation. Whether my abandonment of intraabdominal radiation is a wise step cannot yet be predicted. Possibly deep x-ray will accomplish as much as radon seeds in the destruction of cancer cells that have not reached the lymph glands. At any rate I believe it is imperative that every risk to the operation be eliminated, so that the mortality will be not appreciably greater than the 0.5 per cent attendant upon radiation. Technically the difficulties are not great. I have thus far caused no injury to the large vessels, although the dissection of the lymph glands approximates them closely. We must know when to stop. If the gland is broadly adherent to the vein, it is wiser to desist. In two patients included in this series one such adherent lymph gland was left, although the remainder were removed. In three other cases an exploratory operation showed the lymph gland mass so large and adherent that the operation had to be abandoned. Two of these received intraglandular radiation. There was no mortality in these three cases, but they were of course not included in the present series.

Postoperative complications were infrequent. One patient developed a broad ligament hematoma with subsequent infection that had to be drained from above.

TECHNIC

Naturally the technic of a new operation of this kind will be modified by experience. I have already touched upon the separation of operative measures from radiation treatment. Recently where heavy radiation preceded the operation, I found that the lymph glands were more likely to be adherent and difficult to remove. Hence I would advise the following procedure: Approximately 1,000 to 1,500 r. units of deep x-ray therapy spread over two weeks. Two weeks after this series is concluded iliac lymphadenectomy is done. Two weeks after operation an intrauterine application of 150 mg. radium in gold capsules totalling about 4,000 to 5,000 mg. hours is made. An additional 2,000 to 2,500 r. units of deep x-ray should follow the radium treatment.

Spinal anesthesia which was preferred in the first series, has become routine in the past two years. As a rule 200 mg. of novocaine dissolved in the spinal fluid has been injected. The intestinal relaxation following spinal anesthesia is essential to proper inspection of the pelvic cavity. In cases where ether had to be used to supplement the spinal anesthesia, it was found advantageous to use inhalation of about 25 c.c. of vinethene as an intermediary. This method avoided the struggling that previously was encountered at the beginning of the ether narcosis.

In the operative technic the most important change in the past year has been the additional removal of the glands situated over the external iliac vessels near their exit from the abdominal cavity. These glands are usually enlarged and their removal is relatively easy. How often they are involved in cervical cancer remains to be seen. Cameron Duncan who recently reported a small series of iliac lymphadenectomies suggests routine ligation of the uterine arteries. I cannot agree that this will be without considerable added risk in many cases. Where a ureteral gland must be removed, such a ligation may be necessary but anything that complicates or unduly prolongs the operation must be avoided. The routine removal of all loose fat in the area exposed, as suggested by Duncan, has been done by me in all cases for several years. Abdominal implantation of gold radon seeds has been abandoned for two years as not devoid of dangers and probably not more effective in the destruction of connective tissue extension than a full course of x-ray therapy. The operation requires about one to one and one-half hours for completion.

GLAND METASTASIS

Glandular metastasis in these 46 cases was found 15 times (33 per cent). This is considerably lower than I reported in my first series (44 per cent). The change is evidently due to the fact that almost all patients in the past two years have been subjected to heavy previous radiation treatment. A division of patients receiving little or no radiation and those receiving heavy radiation before operation showed that in 20 unradiated patients, cancer was found 9 times (45 per cent) whereas in 26 preradiated patients, lymph gland metastasis could be diagnosed in only six (23 per cent). From analogy with radiated lymph gland metastasis elsewhere I cannot believe that all

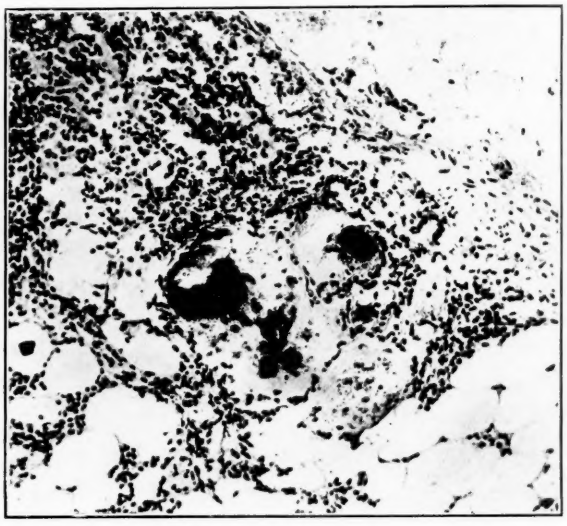


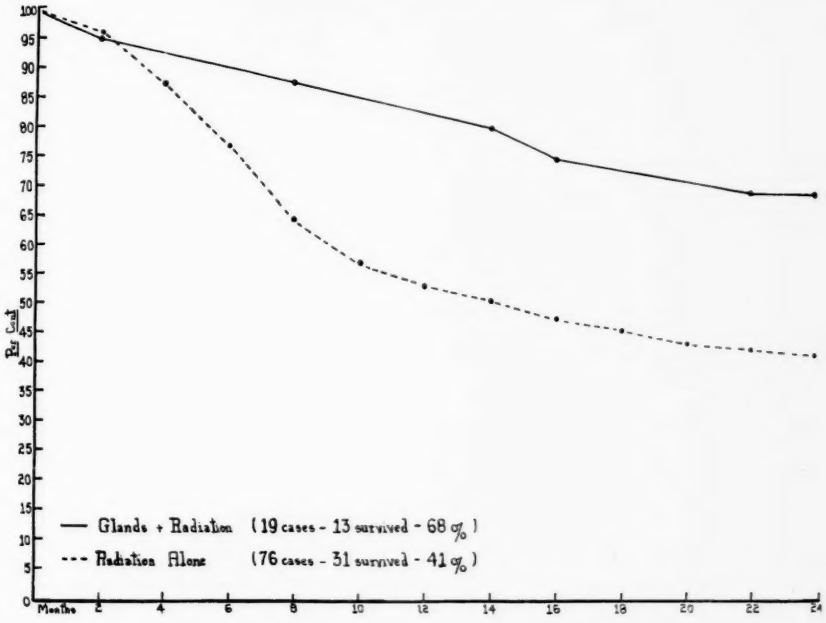
Fig. 1.—Iliac lymph gland, containing a small nest of epithelial cells showing degenerative changes and calcium deposits, that suggest a radiated cancer metastasis.

cancer cells have been destroyed by this preliminary radiation but merely that their recognition has been made more difficult. Occasionally we found areas, as seen in Fig. 1, that strongly suggest an irradiated cancer nest.

A total of 194 glands were removed in these 46 patients and subjected to careful microscopic study. Many unusual conditions were encountered that will be the subject of a later publication. Unfortunately we know too little of the normal and pathologic anatomy of lymph glands. The question whether there was any marked tendency to glandular metastasis in the more anaplastic tumors must be answered in the negative. Out of 43 cases on which data were available the cervical lesion in seventeen was classified as Grade 1 or 2 and showed 5 gland metastases (29.4 per cent) whereas in 26 the cervical

cancer was classified as Grade 3 or 4, and showed 9 metastases (34.6 per cent). One additional case in the former group would have evened the difference.

And now to come to the crux of the problem. What was the survival rate of patients treated by this method and how does it compare with the survival rate of patients of the same group treated in the same institution by radiation alone? Since only two patients had been operated upon more than five years ago, I had to content myself with an analysis of two-year and four-year survivals. I realize that even here we are dealing with small numbers, and it would be dangerous

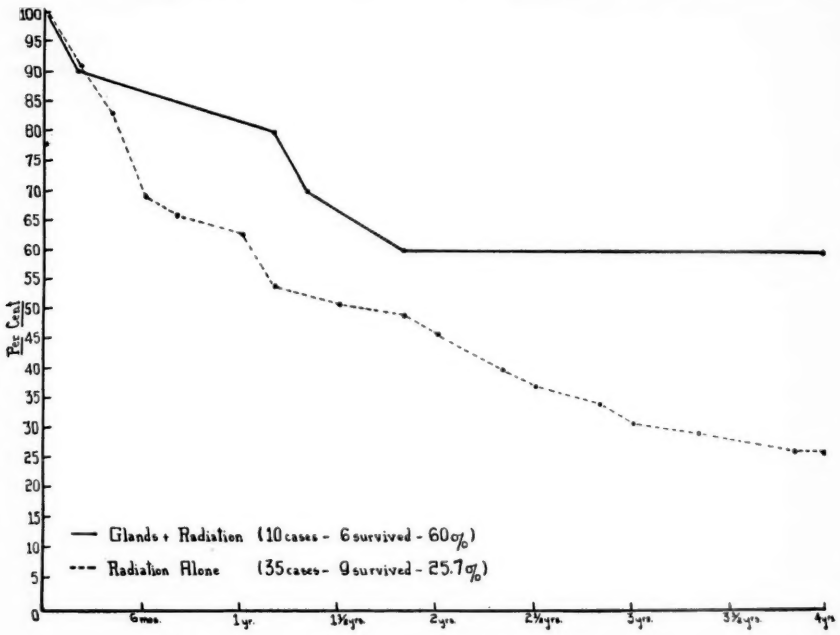


Graph 1.—Two-year survival curve.

to draw any positive conclusions. Nevertheless the difference in results obtained is so striking that I feel encouraged in continuing this plan of treatment and recommending it for trial by others. In Graph 1 the 19 patients operated upon two years or more ago are compared with 76 patients treated with a similar dose of radiation but without lymph gland removal in our hospital during this same period of time (October, 1930 to April, 1934). Except for the first drop due to operative mortality, the survival curve remains definitely higher in the group of lymphadenectomies. In Graph 2 we see the survival curves of patients treated over four years ago, ten lymphadenectomies with radiation, compared with 35 patients whose cancer showed the same stage of involvement not operated upon but radiated by the same

method during the same period of time (October, 1930 to April, 1932). The percentage of survival in the operated cases was found to be approximately twice as great as those receiving radiation alone.

Unfortunately any new method of treating cancer must combine a large experience over a long period of time before drawing even tentative conclusions. If the favorable results thus far obtained in the treatment of borderline cancer of the cervix will encourage others to give this operation a trial, we may before long have an answer to our problem. My experience of the past five years has convinced me that iliac lymphadenectomy in the hands of a competent surgeon, done upon patients that are good operative risks with only partial cancerous



Graph 2.—Four-year survival curve.

involvement of the broad ligaments, is a relatively simple and harmless procedure and gives an increased chance of survival and cure that definitely justifies this surgical intervention.

3720 WASHINGTON AVENUE

DISCUSSION

DR. WILLIAM P. HEALY, NEW YORK, N. Y.—Naturally Dr. Taussig has had to choose favorable cases, favorable for surgical intervention. That may make a little difference in the small series, in end-results. Our clinical grouping, in cancer of the cervix, into early, borderline, advanced, and palliative cases, is a very unsatisfactory classification, because so-called early cases have died within the first year, indicating they could not have been early, and cases that have been labeled palliative have gone into a five-year cure group. We are handicapped by the fact

that about 40 per cent to 45 per cent of the apparently favorable cases, according to Bonney's experience, have parametrial lymph gland involvement. That explains the figures for the end-results we get with treatment by radium and x-ray. Most of the cases with a small cervical lesion will give about 80 per cent of five-year cures, but the less favorable cases will drop the results down so that we average in early cases about 55 per cent to 65 per cent five-year cures, which corresponds to the percentage of cases without lymph gland involvement.

Only one in three of Dr. Taussig's cases had gland involvement and they were therefore relatively early and favorable cases for cure. With radiation alone he could get a fair percentage of cures.

I had the privilege of seeing Dr. Taussig operate some years ago upon a patient who had not as yet been irradiated, which I thought was very unfortunate. Dr. Taussig now suggests, and I think rightly, that before any surgical procedure is carried out the patient should have preliminary deep x-ray therapy up to, we will say, 1,500 roentgen in each field, I hope in six fields, two anterior, two posterior, and two lateral. And then in six weeks he will do the operation and two weeks later apply radium. I still think it is a mistake to do the operation before radium has been applied and before the primary lesion has been completely destroyed by radiation.

Four months after radiation with roentgen ray and radium is completed a supracervical hysterectomy may be performed without disturbing the cervical field at all, but with the cleaning out of both broad ligaments. It will be a relatively simple procedure, and you will have done it at a time when probably there is complete quiescence in the lymphatic field as far as active cancer cells are concerned. Nevertheless you will have violated a very important rule of radiation therapy because you will have destroyed lymphatics that have become fibrosed by radiation. While you will undoubtedly take out some cancer, you will, on the other hand, have opened up fibrosed areas on the borders of your incision which would have probably kept the cancer locked up indefinitely. I think you will not, in the final analysis, add anything to the total salvage by any modified surgical procedure or by anything short of a Wertheim operation preceded by irradiation.

I have a specimen taken from a borderline case of carcinoma of the cervix, a young woman forty-one years of age, treated by deep x-ray therapy, 2,400 roentgens to each of four fields, followed by radium. For fifteen months she was free from any evidence of disease, and then on the rectovaginal septum there was found a local recurrence which responded to radiation with radium. The pelvis at no time showed any evidence of recurrent disease, but last December, which was about twenty-two months following her primary treatment, the patient began to have backaches and pains in her legs, and about ten days ago she developed complete anuria. The only thing that we had been able to find between last December and the time of her death was an impression of gland masses along the spine, on each side of the lower abdomen. When she came into the hospital with complete urinary suppression, ureteral catheters were passed and 80 ounces of urine was obtained in twenty-four hours, and then the ureters closed down again completely. There were solid cancer masses on each side of the spine and in the retroperitoneal glands, huge kidneys, and a very sharp angulation in the ureter on the left side from that gland mass. The pelvic fields had been completely taken care of by radiation, and there was no evidence of disease in the uterus or pelvis at the postmortem. I think there is little question that our present methods of irradiation and our ability to take care of these peritoneal lymphatics are becoming more and more satisfactory without going on to surgery.

DR. FRANK W. LYNCH, SAN FRANCISCO, CALIF.—Dr. Taussig is helping us learn the frequency of involved glands concerning which we know little. The observations of Schauta many years ago merely showed that glands were rather frequently in-

volved in the autopsy material he was studying. Kundrat, Kermauner, and Sampson subsequently worked in this field. Aside from these, no one has done much of importance except Comyns Berkeley and Victor Bonney.

Dr. Taussig's resection of glands may prove of value therapeutically. The method is well worth trying, since we are curing about as many cases with radium and x-ray as we are ever likely to do. The longer I follow my cases, the less enthusiastic I am over the treatment of early cervical cancers with radium or x-ray alone. Recently a patient with a very early case died from recurrence seven and a half years after treatment. She had one of the earliest microscopic lesions I have ever seen and was radiated by methods which are proper at the present time. Another patient with a very early lesion died from a heart complication five years after treatment, and at autopsy we found involved glands which had not been recognized clinically. Last year we had two Group III cases of patients well for twelve years, develop recurrences and die thirteen years after treatment.

Unfortunately I have only performed Dr. Taussig's operation five times, all on Group III (A.C.S.) cases. The glands were involved only in two. My follow-up which is complete from treatment to death or survival for nineteen years is teaching me that about all you can expect in treating inoperable cancers is to prolong the life of the patient. If you follow the patients long enough, you will find that they will tend to die from cancer.

The case that Dr. Healy has just reviewed is one of the many new forms of cervical cancer that we have seen since using radium. With radium we tend to cure the local lesion and allow the cancer to grow in places in which we never before have seen it. I have seen fluid in the abdomen and masses in the mesentery that you would be certain were ovarian, yet autopsy proved were cancer that had come from the cervix. I feel that when glands are removed around early lesions that we will not be likely to see cases like this one who died with cancer of the kidney.

DR. TAUSSIG (closing).—In the treatment of cervical cancer we should employ to some extent a comparison with other forms of carcinoma. Take cancer of the breast for instance. Radiation attack on the lymph glands, although in the axilla they lie right under the skin, has failed absolutely. I do not know what happens when cancer gets into the lymph glands, but in some way it becomes more resistant to radiation treatment. When simple mammectomy was done for cancer of the breast, the cures were pitifully rare. Then the radical removal of the lymph glands was begun and although cancer was found only in a limited number of those lymph glands, the percentage of cures was markedly increased. If in only 33 per cent cancer was found, this does not mean that cancer was not present in a very considerable number of the remaining cases.

I feel, therefore, that any surgical lymph gland removal that will supplement radiation without an accompanying high mortality is a justifiable one.

Hamant and Durand: Hysteroscopy, Rev. franç. de gynéc. et d'obst. 31: 1, 1936.

In the opinion of the authors, hysteroscopy now has a definite technic which makes it of practical use. It has no dangers and it is very easy to employ. It is the most certain way to make a diagnosis of intrauterine abnormalities because of direct vision and the possibility of a biopsy. In a short space of time perfected instruments will enable us to employ catheterization of the fallopian tubes. The authors believe hysteroscopy will prove as useful as cystoscopy.

J. P. GREENHILL.

PREMATURE RUPTURE OF THE MEMBRANES AS A MEANS OF INDUCING LABOR*

E. D. Plass, M.D., and C. W. Seibert, M.D., Iowa City, Iowa
(From the Department of Obstetrics and Gynecology, Iowa State University)

DURING the past three years, rupture of the membranes has been employed to complement medical induction of labor with castor oil and quinine, with or without pituitary extract. In the majority of instances there was no medical indication for the induction, which was used as a convenience procedure in an attempt to reduce the period of hospitalization for waiting patients. Only two contraindications, contracted pelvis and abnormal presentation, were recognized. Six hundred and eighty-one records have been studied and form the basis for this communication.

General Data—Parity.—There were 195 primigravidas and 486 multigravidas. In the early period of the work, there was a tendency to limit the procedure to parous women, but more recently it has been recognized that the primiparous cervix rarely offers any real difficulty to instrumental rupture of the bag of waters.

Type of Pelvis.—The pelvis was normal except in 10 patients, who had insignificant degrees of contraction (funnel pelvis 10, simple flat 1, generally contracted 1, and obliquely contracted pelvis of unilateral lameness 1).

Presentation.—There were 672 cephalic and 9 breech presentations, although generally the latter were excluded through fear of prolapse of the cord. Among the former, the occiput was to the left in 384 (57 per cent) and to the right in 288 instances.

Height of Presenting Part.—The presenting part was floating in 335 cases and was fixed but still above the spines in 300 others, leaving only 46 patients with the head actually engaged.

Table I. Height of Presenting Part When Membranes Were Ruptured

Floating	322
Fixed—above spines	300
Engaged—at spines	39
Engaged—below spines	7
No data	13
	681

Condition of the Cervix.—The cervix was completely effaced in only 6 instances, but was thinned to some extent in 42 others, while it was thick and uneffaced in 633. The canal admitted one finger in 468 cases and two fingers in 181 cases, while in 32 instances it was closed necessitating digital or instrumental dilatation before the amnion could be reached.

Complications of Pregnancy.—The pregnancy was normal in 597 instances, while in the remaining 84, there were various complications some of which offered indica-

*Read at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25 to 27, 1936.

tions for the interruption of the pregnancy (eclampsia 1, nonconvulsive toxemia of late pregnancy 45, cardiovascular disease 4, and pyelitis 7) while the remainder were more or less incidental.

Analgesics Employed.—The usual clinic criteria for the administration of analgesics were followed: in 469 cases none was given, but the remaining 212 patients received some sedative drug (morphine and scopolamine 127, morphine 33, barbituric acid preparations 51, and rectal ether and oil 1).

Anesthesia.—Except in 28 instances when the rapidity of delivery made it impossible, anesthesia was employed as usual (ethylene 579, ethylene and ether 25, open ether 38, chloroform 3, local infiltration 7, and spinal 1).

Preliminary and Subsequent Oxytocic Medication.—In only 7 cases was rupture of the membranes employed without preliminary medication given to induce labor. In 333 instances, castor oil and quinine were given alone while in 336 several small doses (2 to 7 minims) of pituitary extract were also administered (usually by hypodermic injection). Quinine was used alone in 5 patients. In 182 instances, painful uterine contractions had begun before the membranes were ruptured and labor would probably have continued even if nothing more had been done.

In 323 cases no medication was given after the membranes were ruptured, but if painful uterine contractions did not appear promptly small doses of pituitary extract were employed. When the latent period was longer than twenty-four hours, the regular medical induction was repeated. In one case where early delivery seemed imperative a Voorhees' bag was introduced.

Technic of Rupture.—The actual technic for rupturing the membranes varied somewhat with different individuals but in general was most easily accomplished with Allis clamps, provided with special long curved handles (overall length 24 cm.) which had been made up especially for this purpose. Vaginal examination was carried out under sterile precautions, and after the bag of waters was punctured, careful exploration was carried out to determine that the cord or an extremity had not prolapsed. Mercurochrome (2 per cent) was poured into the vagina at the conclusion of the manipulation. Patients were not permitted out of bed unless the presenting part was firmly engaged.

Results—Direct.—In only a few instances was there any unfavorable development directly related to the release of the amniotic fluid. There were five prolapsed cords, a higher incidence than should have been noted if spontaneous rupture of the membranes had been permitted; two of these babies were lost and their deaths may be attributed to the procedure. Prolapse of an arm occurred once and demanded later intervention to accomplish delivery. Moderately profuse bleeding occurred once on the basis of a marginal placenta previa, but might have been expected in any event when uterine contractions lengthened the lower segment.

MATERNAL RESULTS

Latent Period.—The period from the rupture of the membranes to the appearance of definite labor pains was less than one hour in 398 patients. Excluding the 183 individuals who were probably in early labor following medical inductions, there were 215 who responded almost immediately to the procedure. On the other hand, the latent period was longer than twenty-four hours in 32 cases (4.7 per cent) with the longest interval eighty-eight hours. In one case, where early delivery seemed imperative, a Voorhees' bag was introduced to stimulate painful contractions.

Prolongation of the latent period beyond twenty-four hours was noted most frequently in those women who had had three or more children, whereas very short latent periods (less than one hour) were less common in primigravidas who nevertheless usually (97 per cent) went into labor in less than twenty-four hours.

TABLE II. THE LATENT PERIOD

	NO.	PER CENT
Less than 1 hour	398	58.4
1 to 6 hours	208	30.5
6 to 24 hours	43	6.3
More than 24 hours	32	4.7
	681	99.9

TABLE III. LATENT PERIOD IN RELATION TO PARITY

NUMBER OF PREVIOUS CHILDREN	LATENT PERIOD									
	TOTALS		LESS THAN 1 HOUR		1 TO 6 HOURS		6 TO 24 HOURS		MORE THAN 24 HOURS	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
None	195	*29*	101	*52*	68	*35*	19	*10*	7	*3*
One	146	*21*	96	*66*	41	*28*	6	*4*	3	*2*
Two	109	*16*	69	*63*	33	*30*	3	*3*	4	*4*
Three to five	155	*23*	94	*61*	44	*28*	5	*3*	12	*8*
Six and more	76	*11*	38	*50*	22	*30*	10	*13*	6	*8*
Totals	681	*100*	398	*59*	208	*30*	43	*6*	32	*5*

Duration of Labor.—Labor was rapid (under six hours) in 56 primiparas (28.7 per cent) and in 297 multiparas (61.1 per cent), and lasted more than thirty hours in 8 primiparas (4.1 per cent) and in 5 multiparas (1.0 per cent). The distribution according to parity is shown in Table IV.

TABLE IV. DURATION OF LABOR IN RELATION TO PARITY

PREVIOUS CHILDREN	TOTAL IN GROUP	0-3 HOURS		3-6 HOURS		6-12 HOURS		12-18 HOURS		18-30 HOURS		MORE THAN 30 HOURS	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
None	195	11	5.6	45	23.1	66	33.8	47	24.1	18	9.2	8	4.1
One	146	31	21.2	61	41.8	41	28.1	11	7.5	2	1.4	0	0.0
Two	109	16	14.7	47	43.1	31	28.4	8	7.4	5	4.6	2	1.8
Three to five	155	39	25.2	55	35.5	43	27.7	12	7.7	4	2.6	2	1.3
Six and more	76	22	28.9	26	34.2	20	26.3	5	6.6	2	2.6	1	1.3
Totals	681	119	17.5	234	34.4	201	29.5	83	12.2	31	4.6	13	1.9

No directly comparative figures are available, but it is obvious that when labor is completed within twelve hours by 62.5 per cent of primiparas and within six hours by 61.1 per cent of the multiparas, the average birth process cannot be considered prolonged.

Method of Delivery.—Parturition was spontaneous in 642 instances (94.3 per cent) even though the usual indications for operative intervention were observed, and several low forceps extractions were done because of complicating maternal disease. Among the primiparas, the operative incidence was 10.8 per cent and in the parous group 3.7 per cent.

Blood Loss.—The average blood loss was 227 c.c., but there were 21 patients (3.1 per cent) who suffered more or less severe postpartum hemorrhages (more than 600 c.c. blood loss). When the latent period was longer than six hours, the incidence of postpartum hemorrhage was considerably increased, but prolongation of labor had the most significant effect.

TABLE V. BLOOD LOSS IN RELATION TO LATENT PERIOD

LATENT PERIOD	TOTAL IN GROUP	BLOOD LOSS					
		LESS THAN 200 C.C.		200 TO 600 C.C.		MORE THAN 600 C.C.	
		NO.	%	NO.	%	NO.	%
Less than 1 hour	398	202	50.8	185	46.5	11	2.8
1 to 6 hours	208	103	49.5	99	47.6	6	2.9
6 to 24 hours	43	20	46.5	21	48.8	2	4.7
More than 24 hours	32	17	53.1	13	40.6	2	6.3
Totals	681	342	50.2	318	46.7	21	3.1

TABLE VI. BLOOD LOSS IN RELATION TO LENGTH OF LABOR

DURATION OF LABOR	TOTAL IN GROUP	BLOOD LOSS					
		LESS THAN 200 C.C.		200 TO 600 C.C.		MORE THAN 600 C.C.	
		NO.	%	NO.	%	NO.	%
Less than 6 hours	354	191	53.9	155	43.8	8	2.3
6 to 18 hours	283	133	47.0	141	50.0	9	3.2
More than 18 hours	44	18	40.9	22	50.0	4	9.1
Totals	681	342	50.2	318	46.7	21	3.1

Puerperal Morbidity.—There were no maternal deaths in the series. The total morbidity rate, based upon a reading of 100.4° F. at any time during the first ten days of the puerperium with temperatures taken every four hours day and night, was 24.1 per cent. In 102 of the 164 febrile patients, the temperature elevation subsided in less than twenty-four hours, leaving a more-than-one-day fever incidence of 9.1 per cent. In only 7 instances (1.0 per cent) did the fever persist for more than one week. There were 17 patients (2.5 per cent) in whom the fever was ascribed to extrapelvic conditions; it is our policy to attribute all febrile reactions to pelvic infection unless there is satisfactory clinical evidence to the contrary, even though there may be no signs of pelvic involvement. It is evident from Table VII that, primiparity and prolongation of the latent period and of the length of labor are definite factors in the production of febrile reactions. Other statistics from the clinic, although not strictly comparable, suggest that the incidence of mild uterine infection is slightly higher in this series, probably by reason of the fact that each patient was subjected to at least one vaginal examination.

TABLE VII. POSTPARTUM FEVER IN RELATION TO VARIOUS FACTORS

HIGHEST POSTPARTUM TEMPERATURE	PREVIOUS CHILDREN				LATENT PERIOD				DURATION OF LABOR			
	NONE		1 OR MORE		UP TO 6 HOURS		MORE THAN 6 HOURS		UP TO 12 HOURS		MORE THAN 12 HOURS	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Under 100.4° (517 cases)	133	68.2	384	77.0	463	76.4	54	72.0	430	77.6	87	68.5
100.4° or more (164 cases)	62	31.8	102	23.0	143	23.6	21	28.0	124	22.4	40	31.5
Totals	195		486		606		75		554		127	

Fetal Results.—There were 29 premature babies (under 2,500 gm.) mostly from patients who presented medical indications for intervention, and 53 children of over 4,000 gm., the largest of which weighed 5,200 gm. The average birth weight was 3,320 gm. There were 11 stillbirths (1.62 per cent) and 10 neonatal deaths (1.47

per cent) with 9 of the fatalities occurring among the 29 premature infants. Among the 652 children, weighing more than 2,500 gm., there were 12 fatalities (1.8 per cent). The assigned causes of death in the two groups, based largely on autopsy findings, are shown in Table VIII.

TABLE VIII. ASSIGNED CAUSES OF STILLBIRTHS AND NEONATAL DEATHS

BIRTH WEIGHTS (GM.)	CAUSES OF STILLBIRTHS					CAUSES OF NEONATAL DEATHS				
	MATERNAL TOXEMIA	HYDROCEPHALUS	INTRACRANIAL HEMORRHAGE	PROLAPSE OF CORD	PREMATURITY	PREMATURITY	INTRACRANIAL HEMORRHAGE	CONGENITAL MALFORMATIONS	ATELECTASIS	HEMORRHAGIC PNEUMONIA
Up to 2,499 (29 cases)	2	1	1	1	1	0	1	1	0	0
2,500 to 3,999 (599 cases)	2	0	2	1	0	1	3	1	1	1
4,000 and more (53 cases)	0	0	0	0	0	0	0	1	0	0
Totals	4	1	3	2	1	1	4	3	1	1

Intracranial hemorrhage, with 7 deaths, heads the list, with congenital malformations, maternal toxemia, and prematurity occupying their usual dominant positions. Only the two fetal deaths ascribed to prolapsed cord can reasonably be charged against the method of induction of labor and such accidents occur even when the membranes rupture spontaneously. One funic prolapse occurred in a patient with a breech presentation. Study of the method of delivery in the cases which resulted in loss of the baby emphasized again the risk of breech extraction, where the uncorrected mortality was 5, or 56 per cent. One other baby died during a midforceps extraction, while in the remaining 15 deaths the deliveries were spontaneous.

TABLE IX. STILLBIRTHS AND NEONATAL DEATHS IN RELATION TO LATENT PERIOD

LATENT PERIOD	TOTAL IN GROUP	STILLBIRTHS		NEONATAL DEATHS		TOTAL DEATHS	
		NO.	%	NO.	%	NO.	%
Less than 1 hour	398	3	0.75	8	2.01	11	2.76
1 to 6 hours	208	4	1.92	1	0.48	5	2.40
6 to 24 hours	43	3	7.00	0	0.00	3	7.00
More than 24 hours	32	1	3.13	1	3.13	2	6.26
Totals	681	11	1.62	10	1.47	21	3.09

TABLE X. STILLBIRTHS AND NEONATAL DEATHS IN RELATION TO LENGTH OF LABOR

DURATION OF LABOR	TOTAL IN GROUP	STILLBIRTHS		NEONATAL DEATHS		TOTAL DEATHS	
		NO.	%	NO.	%	NO.	%
Less than 6 hours	354	5	1.41	5	1.41	10	2.82
6 to 18 hours	283	5	1.77	4	1.41	9	3.18
More than 18 hours	44	1	2.27	1	2.27	2	4.54
Totals	681	11	1.62	10	1.47	21	3.09

Prolongation of the latent period definitely increased the risk to the infant (Table IX) with intracranial hemorrhage accounting for three of the 5 fatalities, although in two instances the labor was completed in less than six hours.

In general, the fetal and infant mortality increased as the duration of labor was prolonged.

Among the primiparas, the fetal loss was 4.1 per cent, and among the parous patients, 2.2 per cent. In the former group, maternal toxemia and intracranial hemorrhage led the causes of death.

DISCUSSION

This considerable experience with the induction of labor by rupture of the membranes combined with the administration of the commonly employed oxytocic agents has led to the belief that it is more effective and less harmful than other recognized mechanical procedures previously recommended for the same purpose. Its simplicity is indicated by the fact that some dozens of internes with little experience carried out the prescribed technic in the large majority of these cases without serious accident to the mother, and with no more than two infant fatalities that could be attributed to the procedure. In 95 per cent of this series, labor was inaugurated within twenty-four hours after the membranes were ruptured, and was completed in no longer than the anticipated time. In spite of the fact that the presenting part was unengaged in 335 instances, there were only 5 prolapsed cords.

Deliberate rupture of the bag of waters prematurely has made it necessary to change our conceptions of the difficulties of "dry labor," which were formerly stressed and to conclude that dystocia under such circumstances must be due to some other factor such as uterine inertia, faulty mechanism, or abnormality of the bony pelvis. Moreover, it has been necessary to revise our ideas of the mechanism of cervical dilatation by minimizing the effect of the "dilating hydrostatic wedge" principle and emphasizing rather the pulling up of the lower segment by the shortening uterine body and the contractions of the longitudinal fibers of the isthmus and cervix.

CONCLUSIONS

The induction of labor by premature rupture of the membranes after stimulation of the uterus through the action of castor oil, quinine, and pituitary extract is safer than the other forms of mechanical irritation employed for this purpose (bougies, bags, or packing). Although the risk to the mother and child is very small, the procedure should be recommended only when there is a definite indication for termination of the pregnancy.

DISCUSSION

DR. LEIGHTON C. CONN, EDMONTON, ALBERTA, CANADA (By Invitation).—The frequency with which this method is used in my country is shown by the following percentages. Of 1,707 general admissions to the Vancouver General Hospital this method was used 51 times. In our own University Hospital, this maneuver was used 94 times in 1,000 consecutive admissions, while in the Royal Alexandra Hospital in a similar series it was performed 17 times. In the Royal Victoria Hospital,

Montreal, through 1,000 consecutive admissions, rupture of the membranes was performed in 75 instances. The latent period in these several series averages 3.5 hours while the duration of labor averages 7.5 hours.

The slides of our own series of cases show the indications for rupture of the membranes to be: preeclamptic toxemia 48 cases, disproportion 38 cases, hydramnios 3 cases, hemorrhage 3 cases, and twins 2 cases. In 16 cases we used rupture of the membranes alone, while in 30 cases we gave a medical induction prior to rupturing the membranes. In 44 cases where medical induction failed, we allowed an interval to elapse before rupturing the membranes; which I think is a mistake. In 4 cases where medical induction followed by bag insertion had failed, the membranes were ruptured to induce labor.

The latent period varied with the procedure used, whether rupture was performed alone or followed medical induction. The duration of labor in our series is greater, I think, than in the cases presented by Dr. Plass. In 20, outlet forceps were applied, while in 13 cases manual rotation of the head followed by forceps application was necessary to effect delivery.

Rupture of the membranes would appear to offer an effective means for the induction of labor but, to me, there are some dangers. In spite of the large number of cases where Dr. Plass used this method in the presence of a floating head, I still believe there will result an occasional prolapsed cord. In the primipara with a long cervix, where one would have to dilate the cervix in order to rupture the membranes, there is a greater tendency for a longer latent period. As Dr. Plass has shown, if there is a longer latent period there is greater danger of morbidity to both mother and child. In these cases we do not perform this method of induction.

In reviewing the records, I was struck with the instances in which, following rupture of the membranes, the interne had noted "tumultuous pain." Is it not safer for the baby in these severe types of labor to keep the head surrounded by the bag of waters so that the pressure will be more evenly distributed thereon?

Moreover, while in the acutely toxic cases labor ensued quickly, in the chronic types of toxemia we had extreme difficulty in getting the uterus to contract. In the latter I prefer the following method: first to insert a bag to secure sufficient dilatation and then, if necessary, to rupture the membranes.

I feel that one should have a definite indication for bringing on labor. In Dr. Plass' hands and in his clinic there would perhaps be no difficulty but, if we were to have this tried throughout the country, I believe that both fetal mortality and maternal morbidity might be increased. We did not lose any mothers in our series and our maternal morbidity, by the same standard, was only 11 per cent. This, I feel, was rather a matter of luck as the number of cases was very small. I would consider rupture of the membranes, where indicated, an excellent procedure, but we must bear in mind that there are times when it is neither safe nor effective.

DR. NICHOLSON J. EASTMAN, BALTIMORE, MD. (By Invitation).—The report of Dr. Plass on the induction of labor by artificial rupture of the membranes has seemed to me most interesting and instructive, for he has disregarded completely what I have always taken to be the two main contraindications to the method, namely, a floating head and a long, hard cervix. In about one-half of his cases the head was floating and in the vast majority the cervix was thick and uneffaced.

When we violate a well-recognized and reasonable contraindication, we expect in a long series of cases to pay a price, and I feel that Dr. Plass has paid a price in his series in the form of five cases of prolapse of the umbilical cord and one case of prolapsed arm. In a series of 303 Baltimore cases quite comparable in other respects to those of Dr. Plass, but in which we were careful not to employ this procedure unless the head was engaged, there was only one case of prolapsed cord. This represents an incidence of 0.3 per cent, whereas in Dr. Plass' series it was approximately 1 per cent. Accordingly, it would seem reasonable to believe that when

we rupture membranes for the purpose of inducing labor in cases in which the head is floating, we impose upon the infant the likelihood of prolapse of the umbilical cord. Now, if the condition prompting the induction, let us say a fulminating toxemia, imposes upon the child a greater danger, this is all very well, and I feel we are very much indebted to Plass for demonstrating the relative safety and feasibility of this procedure under such circumstances. But in the absence of such indications, to rupture the membranes simply for the convenience of the patient or of other persons involved in the case seems to me unjustifiable and at variance with the best interests of mother and child.

Although it is difficult to prove statistically, there is some evidence that the quinine usually employed as preliminary medication to rupturing the membranes may be harmful to the infant, and we have reduced the dosage by degrees from 30 to 20 to 10 to 6 gr. Furthermore, we now have a small series of 50 to 60 cases of labor induced by rupture of the membranes in which no quinine at all was employed; and the procedure seems to work just as well without it. In a series of experimental studies, Schübel has shown that large doses of quinine paralyze the uterus, while small doses of quinine stimulate it; and he finds that the maximum stimulating dose in animals is 1 to 2 mg., intramuscularly, per kilogram of body weight. This would correspond in the human being to a dosage of some 3 to 4 gr. by mouth. In view of this evidence it would seem quite possible to reduce the dose of quinine without decreasing the efficacy of artificial rupture of the membranes, and possibly with some gain in safety to the infant.

DR. CARL BACHMAN, PHILADELPHIA, PA. (By Invitation).—Many obstetricians must feel that Dr. Plass' report, based as it is upon a careful study of so many cases, sets a capping stone upon the evidence which has been accumulating during the past decade in favor of puncture of the membranes. The evidence on the whole would indicate that when this method is applied experimentally by competent men to cases of normal pregnancy at term, it is simple and effective, is probably the safest of the known effective methods of induction, and, barring the accident of prolapse of the cord, entails no serious increase of risk to mother or infant over that to be expected in a comparable group of natural labors.

The studies of Reynolds, Robson and others show that in lower animals uterine motility in pregnancy is inhibited to a marked degree by endocrine factors until shortly before term. Obstetricians have repeatedly experienced difficulty in inducing premature labor. Berger, for instance, with the very method under discussion, found that the latent periods and subsequent labors were usually prolonged when the induction was attempted prior to term. Schulze, furthermore, noted that following spontaneous rupture of the membrane in preterm pregnancies the labors were tedious in spite of the absence of any factors of disproportion or malpresentation.

All of this therefore raises the question whether one may not speak of a necessary irritability or preparedness of the uterus for labor, a condition not arrived at until term. Could the data which Dr. Plass has so carefully analyzed in other respects be recast to correlate the length of the latent period and subsequent labors with the maturities of the pregnancies as indicated by the weight and length of the infants delivered? Would the figures show that prolonged latent periods and labors were associated with the birth of small and presumably preterm infants?

A second aspect of the problem is the view of the lower uterine segment as a trigger zone, stimulation of which serves to induce labor notwithstanding any unpreparedness in the contractile upper portion of the organ. The effectiveness of bag induction in many pregnancies which have to be terminated prematurely is an illustration in point. Also pertinent is the difficulty which many, like Fitz-Gibbon, have reported in inducing even term labor by ordinary medical means when the presenting part, as in multigravidas, is still floating.

Is the effectiveness of simple rupture of the membranes the result of the presenting part descending after the drainage of the amniotic fluid or, since some observers have noted that much fluid drainage is not essential for success, at least by the lower uterine segment having been brought into closer contact with the presenting part?

Dr. Plass' data are exceptionally complete and detailed regarding the level of the fetal head at the moment of puncture of the membranes. It would be of great interest if the records could also tell what happens to the head of the fetus or to the lower uterine segment following puncture, particularly toward the end of the latent period and at the onset of effective uterine contractions.

DR. HARVEY B. MATTHEWS, BROOKLYN, N. Y.—There are several points I would like to make. First, in our clinic, we do not rupture the membranes except on indication. Second, regarding the question of morbidity, Dr. Plass spoke of using 2 per cent mercurochrome. We believe that 4 per cent mercurochrome would cut down his morbidity of 24.5 per cent or that of 9.3 per cent, at least in half. We do not ask him to use mercurochrome, but we do advise the use of some potent germicidal agent, because we are convinced that it has something to do with reducing morbidity and mortality. Last, Dr. Plass did not give us the follow-up on the condition of the cervix in these cases in which the membranes have been prematurely ruptured. Such a follow-up would be very interesting.

Would Dr. Plass express his views on the routine premature rupture of the membranes in private practice? Does he recommend such a procedure to the profession?

DR. ALFRED C. BECK, BROOKLYN, N. Y.—It would be interesting if Dr. Plass would inspect the cervices of those cases that can be brought back for observation and compare his findings with those made upon a similar number of primiparas and multiparas who have had labors in which the membranes remained intact for most of the first stage.

DR. EDWARD A. SCHUMANN, PHILADELPHIA, PA.—I cannot refrain from taking one moment in this discussion to assist Dr. Plass in answering Dr. Beck's question. In a series of cases we have rather carefully inspected the cervix during and after labor, and we found that our incidence of laceration is slightly less than in the primipara where the membranes have not been previously ruptured. We do not use mercurochrome in the vagina.

DR. PLASS (closing).—This work was done on a completely experimental basis, as a clinical study. Rupture of the membranes is an efficient means of inducing labor, but I believe it should generally be used only in cases where there is an indication for the interruption.

The effect of small doses of quinine, which Dr. Eastman has mentioned, is very interesting. We have always used from 18 to 20 gr., but I am perfectly willing to reduce the dosage to 2, 4, or 6 gr. with the hope that the results may be as good.

I cannot answer Dr. Bachman's question about the latent period in relation to the weight of the baby.

The question of morbidity that Dr. Matthews raised is a perennial obstetric discussion. If he takes temperature as we do his cases are comparable, but if not comparison is unwise. Our temperatures are taken every four hours, day and night. A four-hour nursing schedule is in effect and temperatures are taken at the same time.

A STUDY OF ONE THOUSAND PLACENTAS*

W. Benson Harer, M.D., F.A.C.S., Philadelphia, Pa.

ALTHOUGH great interest has been shown in the study of placental pathology during the past few years, much still remains to be worked out, and there are still many conditions of the placenta about which there are differences of opinion. A careful analysis of the work already reported by various investigators would probably serve to reconcile some of these diverging opinions, and additional studies of the placenta will surely solve some of the remaining problems. In the hope that additional light might be shed upon this interesting phase of pathology, a combined clinical and pathologic study of the placenta was started in 1934 and has been carried on ever since.

The method of study was as follows: All placentas were examined as soon after delivery as possible and in all cases within twenty-four hours time. After removal of all retroplacental clots and free blood, each placenta was weighed and measured in its smallest and its largest diameters. It was then carefully inspected for any gross abnormalities. The placenta was then spread out on a dissecting board with the maternal surface uppermost and cut through its entire thickness down to the amnion in strips 1 cm. wide. These cut surfaces were examined grossly for abnormalities and the placenta was measured through its thickest portion. It was then cut at right angles to the first series of cuts, so that it was finally divided into blocks 1 cm. square all held together in proper relationship by the amnion and chorion. Sections for histologic examination were taken from appropriate places and prepared by the usual formalin-paraffin technic. It was not possible to prepare histologic sections of all placentas examined. However, care was taken to get a sufficient number of sections from all the different abnormalities noted, and these are still being studied as opportunity permits. The clinical data required to complete the study were then obtained from the hospital records.

All of the patients were white women. The cases were about equally divided between private and ward patients, but, with few exceptions, all were given about the same prenatal care. Practically all of the cases were planned admissions, and all were beyond the twenty-sixth week of gestation. An exceptionally low incidence of clinical abnormalities made this series of cases unusually valuable for a study of the physiologic changes in the placenta in late pregnancy.

*Read by invitation at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25 to 27, 1936.

TABLE I. GROSS ABNORMALITIES OF THE PLACENTA

CASES	NO. OF CASES
Infarcts (5 mm. or larger)	416
Placentosis	226
Cysts	116
Hemorrhage	78
Fibrosis and calcification	104
Placentas showing average pathology	650 (65%)
Placentas showing excessive pathology	350 (35%)

A great deal has been written about placental infarcts, and there is still wide divergence of opinion as to their etiology and their varieties. Williams describes six separate types. Siddall and Hartmann describe four distinct varieties, which they simply number for want of descriptive names. My own opinion is that we should divide them into two classes, maternal and fetal, according to the tissue in which the pathologic changes originated and which is, therefore, most involved. The color of the infarct is of no value in determining its origin. Consequently, it is useless to divide them into so-called red and white infarcts. The color of the infarct depends upon a number of factors, chief among which are the presence or absence of hemorrhage into the affected tissue and the time of occurrence of the pathologic change, before delivery. We may, therefore, have an old white infarct of definite maternal origin which is grossly indistinguishable from the more commonly occurring fetal white infarct in which the chorionic villi are chiefly affected. The incidence of infarcts in this series (41.6 per cent) was lower than that reported by most other observers.

During the stage of formation of the placenta and for a short time after a definite hemotrophic system of nutrition is provided for the embryo, the enzyme from the trophoblast liquefies and holds in a state of liquefaction the maternal cells with which it comes in contact. At this stage the trophoblast is markedly invasive, but as soon as the secondary villi are formed and vascularized, its invasive properties slow down and apparently its enzymic action ceases. Up to this point there have been marked destruction of the decidua and lesser injury to the trophoblastic tissue. Wherever tissue damage occurs, it is nature's rule to wall-off the damaged or dead tissue from the adjacent normal tissue. This is accomplished by the deposition of fibrin and the invasion of the area by neutrophiles, erythrocytes, lymphocytes, and reticulo-endothelial cells. In other words, the phenomenon known as an inflammatory reaction takes place around or in the damaged tissues. In the placenta, however, the enzyme action of the trophoblast resists this for a time. Likewise the syncytial cells possess the characteristic of endothelium in not instituting clotting of blood. As the placenta grows older, the enzyme action is lost and degenerative changes occur in the syncytial cells, so that they no longer inhibit but now actually cause the deposition of fibrin. This is, of course, the explanation of the formation of Nitabuck's fibrin

layer, but I believe it is also the explanation of the formation of most of the so-called white infarcts of the placenta, especially those of rather irregular outline, involving chiefly the chorionic villi. Here the fibrin is deposited in little masses on and under the syncytium of the villi. As a result, the function of the villus is interfered with and eventually it undergoes necrosis. This process, going on simultaneously or progressively in a group of adjacent villi, results in the formation of an infarct which, because of the relative absence of hemorrhage into the affected area, is white from the start. Practically every placenta at term shows numbers of such infarcts of various sizes. I believe they represent purely senile changes and, except for the fact that such a placenta, like any other senile organ, is abnormally suspectible to changes from any other disease condition, bear no relation to toxemia in the mother. A striking and, to me, significant feature in connection with such infarcts is the relative absence of enmeshed red blood cells in these fibrin masses and the almost complete absence of neutrophiles and lymphocytes around these necrotic areas. If the necrosis occurs sufficiently early in pregnancy for nature to fibrose the affected area, then one sees reticuloendothelial cells invading the necrotic areas but not in such large numbers as are commonly seen in infarcts of other organs, such as the kidney, and not accompanied or preceded by neutrophiles and lymphocytes. I interpret this to mean that such infarcts are of a very low degree of toxicity to the surrounding more normal tissue and to the maternal organism.

The deposition of fibrin around senile and consequently degenerated villi is, therefore, the primary factor in the production of so-called white infarcts of the placenta, and the endarteritis, thrombosis, and hemorrhage seen in such infarcts are secondary to the added interference with villous function by this fibrin deposit.

As the hormonal stimulation of the decidua begins to fail, this structure also undergoes degenerative changes. From a maximum thickness of about 10 mm. at the fourth month of pregnancy, it becomes thinned out to only 1 or 2 mm. at term. Part of this thinning of the decidua is due to the growth of the uterus, but much of it is due to actual regression and degeneration of the decidua. At any rate, it becomes progressively suspectible to traumatism, toxins, and disease conditions in the mother, so that frequently definite damage occurs in this tissue, and because of the highly vascular character of the decidua, such damage usually results in hemorrhage. Provided the hemorrhage is not too extensive, the pregnancy will continue without clinical evidence of the accident, and at the time of delivery, we will find one of the following pictures, dependent upon the time at which the hemorrhage occurred. If the hemorrhage occurred during or shortly before labor, there will be a sharply circumscribed collection of fluid blood of a red or black color somewhere within the placental substance. If the accident occurs a little

earlier, the blood will be clotted and surrounded by a fibrous pseudo-capsule out of which the clot may be turned intact like a hard-boiled egg may be removed from its shell. In one case in this series, the clot was so perfect that a tiplike process leading into the maternal blood vessel, from which the hemorrhage occurred, could be clearly seen. When still older, we find the clot partly invaded by fibrous tissue, so that it can no longer be cleanly removed from its capsule. In still older specimens, the clot is entirely penetrated by fibrous tissue, and the color at the periphery is gradually removed until finally, in very old specimens, the entire area is converted into a mass of white fibrous tissue, sometimes with a cavity in the center. The placentas in this series presented all these variations in a striking manner. In no case was the fetus affected so that my findings are in complete agreement with those reported by McNally and Dieckmann in 1923. In many of the placentas showing such infarcts, there were immediately adjacent white infarcts of the type first described. This, of course, might logically be expected. In no case, however, was I able to find an infarct which appeared to be of any other origin.

TABLE II. TOXEMIA AND PLACENTAL PATHOLOGY

TYPE OF TOXEMIA	NO. OF CASES	PLACENTAL PATHOLOGY		FETAL MORTALITY
		AVERAGE	EXCESSIVE	
Nephritic	3	0	3 (100%)	1 (33⅓%)
Eclamptic	2	1 (50%)	1 (50%)	1 (50%)
Preeclamptic	14	6 (43%)	8 (57%)	5 (36%)
Totals	19	7 (37%)	12 (63%)	7 (35%)

The number of cases of toxemia in this series (19) was too small to be used in drawing definite conclusions as to the relationship between toxemia and placental pathology. I will, therefore, simply state the facts of these cases and the opinion I have formed from them. Fifteen and one-half per cent of our fetal deaths occurred in toxemic patients. There were three cases of nephritic toxemia in this series. In all three there was very extensive pathology in the placenta. In one patient more than two-thirds of the placenta was infarcted. The fetus was born dead. In another, about 60 per cent of the placenta was infarcted, but a living fetus was delivered. In the third case of nephritic toxemia, the placental pathology consisted of marked fibrosis with calcification of the maternal surface of the placenta and a number of discrete scattered placental infarcts, 5 of which measured at least 5 mm. in diametre. In this case also a living baby was born.

One case of eclampsia showed more than the average amount of placental pathology, and the fetus was born dead. The mother also died of toxemia and postpartum hemorrhage. In the other case of eclampsia, the placenta was about as normal as the average, and the fetus was born alive.

Among the fourteen cases of preeclamptic toxemia, there were 5 stillborn children, including one set of twins. In the case of the twins, there was marked placental pathology with infarcts and senile changes and very thick, short umbilical cords with small vessels, much jelly of Wharton and almost no twists whatsoever. In the other three cases of preeclampsia in which stillbirths occurred, the placental pathology was of more than average extent, but no greater than that seen in a number of placentas from clinically normal cases with the births of living fetuses. In the remaining 10 cases of preeclampsia, 4 placentas showed more than average pathology, and 6 were of average or even a little less than average pathology. Thus, it is seen that in these 19 cases of late gestational toxemia, there were 7 fetal deaths, 4 of which were definitely traceable to placental pathology. Twelve of the 19 placentas (one fused twin placenta) showed pathologic changes exactly similar to but more extensive than those seen in the average normal cases in this series. The remaining 7 placentas were as nearly normal as are usually found at term. Therefore, the incidence of placental pathology among these toxemic patients was 63 per cent as compared with 35 per cent for the entire series. Although considerable time was spent in studying the histologic sections of these placentas, we were unable to find anything whatsoever that would enable us to state that the section came from a placenta of late gestational toxemia. Even the extent of the gross and microscopic changes was of no value in this respect, because with the exception of the one placenta from a case of severe nephritis, there were just as extensive changes noted in other placentas from clinically normal patients. Two competent pathologists who very kindly examined these sections were also unable to identify which ones came from patients with toxemia and which came from normal patients. It would seem, therefore, that toxemia is simply an additional factor in producing the degenerative changes that occur in all placentas in the last trimester of pregnancy, but that the result may be such extensive placental damage as to cause the death of the fetus.

SYPHILIS

There were no fetal deaths from syphilis in our entire series. In fact, there were only 5 positive Wassermann reactions obtained in the entire 1,000 patients, an incidence of 0.5 per cent. In two of these patients, positive Wassermann reactions were obtained both prenatally and from the cord at delivery. Both fetuses were clinically syphilitic. The other 3 patients gave positive cord Wassermann reactions, but the fetuses showed no clinical evidence of syphilis. In none of these patients were we able to diagnose syphilis from the histologic or gross study of the placenta. The incidence of syphilis in these patients was very low but is accounted for by the fact that we were dealing with married white women exclusively, and all were of a fairly high social and moral status.

All patients had cord Wassermann and Kahn tests done, and all ward patients and most of the private and semiprivate patients had prenatal Wassermann tests in addition.

PLACENTOSIS

The condition of the placenta described by Goodall under the name of placentosis was encountered in 226 patients in this series. In no case could we find clinical evidence of the presence of this condition before delivery of the placenta. Such a placenta presents a gross picture that attracts immediate attention. It is very dark, almost black in color, thicker than the average with swollen, turgid, well-marked cotyledons. The placenta feels soft, friable as though filled with fluid. The fetal vessels are filled with blood. When cut in the fresh state, the contained blood oozes from the cut surface and after draining away leaves a honeycomb appearance in the placenta. Definite areas of hemorrhage are frequently seen in such placentas. To this picture Goodall has aptly applied the term "red hepatization of the placenta." Although such a condition as just described was encountered in nearly 25 per cent of these cases, there was not a single case in which the condition was as extensive or the placenta as thick as those described by Goodall. The thickest placenta in this series measured exactly 4 cm., whereas Goodall reports placentas of 5 to 7.5 cm. in thickness. Furthermore, we did not encounter a single placenta of the large, white, fattily degenerated type which he describes as the end-result of massive and intense placentosis with death of the fetus. It must be emphasized that the cases in this series presented very few clinical abnormalities and that, therefore, the placentas might logically be expected to be fairly normal. Dr. Goodall's series apparently presented a much higher incidence of clinical and consequently of placental abnormalities. Because of these facts, I have been led to interpret this condition of placentosis very differently than he did. My study of these placentas has resulted in a rather definite opinion that the condition described as placentosis is really simple passive congestion of the placenta. I believe it may be produced by toxic conditions in the mother, although I was unable to find evidence of it in this series. I believe the majority of these cases are caused by interference with the maternal blood supply to the placenta and are due to a reduction in the area of the placental site. This may be brought about in several ways, but the condition is probably most commonly due to our method of handling the third stage of labor. In our hospital the routine method of treating the third stage of labor is to clamp the cord with two hemostats and cut between them. Then an ampule of pituitrin is administered by hypodermic injection and the uterus held with firm, constant pressure until evidence of placental separation appears, at which time it is expressed by suprafundal pressure. Now just what is occurring in the uterus and placenta at this time? First, the fetal circulation

is stopped immediately by the clamping of the cord. The function of the chorionic villi may, however, continue for an appreciable time after the cord is cut. Hence the fetal vessels may become progressively engorged, not with additional cells but with serum from the maternal blood sinuses. Second, the maternal portion of the placenta, although most commonly quickly detached from the uterine wall following delivery of the child, may remain attached and therefore continue to function for some time after the cord is cut. Last, the placental site is being rapidly diminished by the contraction and retraction of the uterus. This results in constriction of the maternal vessels in the placental site, but the effect of the constriction is necessarily more pronounced in the veins than in the arteries. Hence blood is still rather freely entering the placenta, but its egress from the placenta is practically stopped. Here, then, we have all the elements necessary for the production of passive congestion of the placenta. Much the same set of conditions prevails in cesarean sections in which it is common practice to administer oxytocics just before opening the uterus and in which there is frequently a sufficiently long interval between the actual delivery of the child and the removal of the placenta for a passive congestion to occur in this organ. Undoubtedly, there are other methods of production of passive congestion of the placenta. Thus premature rupture of the membranes with loss of much of the liquor amnii and consequent diminution of the area of the placental site might produce it. Hence the condition should be encountered frequently in clinics where the Slemons method of induction of labor is commonly practiced. Likewise, it might be expected to occur rather frequently in that portion of the placenta supplying the second-born child of a twin pregnancy, and this was actually noted in this series of cases. Now if this hypothesis of the production of placentosis is correct, then such a placenta, theoretically, should show the microscopic evidence of passive congestion and such was actually the case. In all such placentas, there is marked engorgment of the fetal vessels and also of the maternal blood sinuses, and the microscopic picture of simple passive congestion was not more frequently complicated by associated, but etiologically unrelated, pathologic changes than would be expected on the basis of the frequency of these associated changes occurring alone. Furthermore, if this hypothesis is correct it should, within certain limits, be possible to control the production of this condition. In an attempt to prove the correctness of this hypothesis, I have been examining a series of placentas from cases in which the treatment of the third stage of labor has been greatly modified. In these cases (all ward cases), a single hemostat is placed near the fetal end of the cord and the cord then is severed and allowed to drain. The uterus is not touched, but the drapes are pulled back so that it may be observed through the abdominal wall. No oxytocics are administered. When there is definite evidence of separation, the placenta is expressed by suprafundal pressure, if necessary;

otherwise it is allowed to be expelled spontaneously. So far, in a series of 43 cases, I have not encountered a single case of placentosis. It is true that only clinically normal patients with normal labors have been utilized for this study, but so far the results bear out my idea that placentosis is simply passive congestion of the placenta which ordinarily is of no clinical importance. However, I fully agree with Dr. Goodall that in the event this condition of passive congestion is present over a sufficiently long period of time before delivery of the child, it may lead to marked definitely pathologic changes in the placenta, such as large areas of infarction, large hemorrhages or even fatty degeneration of the placenta and may so seriously interfere with its function as to cause the death of the child.

SUMMARY

The placentas from 1,000 consecutive deliveries of married, white women beyond the twenty-sixth week of pregnancy were examined grossly in the fresh state within twenty-four hours after delivery. Histologic sections of the abnormalities found were prepared and studied microscopically.

Placental infarcts are classified as fetal and maternal, depending upon the tissue in which the process starts and which is, therefore, most involved. The formation of the placental infarcts is discussed.

A study was made of the relationship between late gestational toxemia, fetal deaths, and placental pathology as evidenced in this series of cases.

The condition known as placentosis is discussed as to its pathology and etiology.

CONCLUSIONS

The occurrence of a high percentage of pathologic changes in the placentas from a group of patients with an unusually low incidence of clinical abnormalities leads to the conclusion that such changes must be considered as senile degenerative changes taking place in an organ whose life span is barely sufficient for the proper performance of its physiologic functions.

The placental changes found in cases of late gestational toxemia are identical with, but occur more frequently, and are more extensive than those found in clinically normal cases. The maternal toxemia must, therefore, be regarded simply as an additional source of injury to an organ already undergoing the pathologic changes incident to senility.

Placental infarcts of the fetal type are due to degeneration of the syncytial cells of the chorionic villi with the deposition of fibrin masses around the villi. These fibrin masses interfere with the function of the villi and so induce endarteritis, thrombosis, and necrosis of the affected villi. An unusual type of low-grade inflammatory reaction occurs around and within the affected tissue and forms the so-called white infarct of the placenta. Placental infarcts of the maternal variety are

due to degenerative changes in the decidua in which, because of its highly vascular nature, hemorrhage is the most characteristic pathologic change. The walling-off and eventual fibrosis of the area form the so-called red infarct of the placenta.

The condition known as placentosis was found in nearly 25 per cent of the placentas in this series. In no case could symptoms or clinical evidence of the presence of this condition be found. It was apparently without effect upon either the mother or the child. The conclusion is reached, therefore, that this condition is one of simple passive congestion of the placenta which in most cases occurs late in labor or even after the birth of the child.

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1900 Rittenhouse Square

DISCUSSION ON PAPERS BY DRS. IRVING* AND HARER

DR. A. T. HERTIG, Boston, Mass.—In some manner, not always apparent, nature has performed an experiment on these uteri which has resulted in the absence, either complete or partial, of decidua, thereby leading to the clinicopathologic entity of placenta accreta. The study of these abnormal placental sites enables us to evaluate some of the disputed histologic features in the normal placental site since one of the normal elements, decidua, is absent. These disputed points are: the fibrinoid layer of Nitabuch, the placental septa, and the placental site giant cells.

The fibrinoid layer of Nitabuch, as has been shown, is associated with the junction of placental trophoblast and maternal decidua. Furthermore, it seems to be a

*To be published in Surgery, Gynecology and Obstetrics.

product of the decidual cells *per se* because strands of this fibrinoid material from the main layer run down, around, and between the true decidual cells. When the latter are absent, the fibrinoid layer is also absent.

As for the placental septa, there are various ideas concerning their origin. Some authors maintain that they are entirely fetal in origin, others say that they are purely decidual in origin, while still others postulate a combined fetal and maternal origin. It would seem, therefore, that when decidua is definitely absent we have a chance to determine the nature of placental septa. In a large proportion of this series where placental septa were available for observation, these structures were composed of varying proportions of trophoblastic cells from the placenta and smooth muscle fibers from the myometrium. Hence, it would seem logical to suppose that these placental septa are derived, in part at least, from the tissue in which the ovum happens to be embedded. In the normal implantation site it is decidua, whereas in such cases as these of placenta accreta where decidua is partially or completely absent, it is myometrium. This finding would, therefore, favor the view that placental septa are of combined maternal and fetal origin.

The two views about the nature of the placental site giant cells are that they are either of trophoblastic or decidual origin inasmuch as those are the only two types of tissue in that region. Since there are none of the decidual cells found in any given area showing the pure picture of placenta accreta, but many placental site giant cells in the underlying myometrium, it would appear to be very good histologic proof that they are of trophoblastic origin.

DR. ARTHUR H. CURTIS, CHICAGO, ILL.—I would like to ask Dr. Irving whether uterine fibroids are a factor in placenta accreta?

DR. IRVING (closing).—I wish to remark about the point brought out by Dr. Dickinson in regard to the location of the placenta. Beginning with the first of the year we have had the distance from the edge of the placenta to the hole in the membranes measured, in an effort to find out where the placenta is implanted normally. With about 2,700 deliveries a year, eliminating the badly torn membranes, we hope in four or five years to have some information that will be useful.

A review of the literature may throw some light upon the implantation and why placenta accreta occurs. The site was noted in 58 cases. The placenta was implanted in the corpus, which we believe is the normal site, in 19 cases, and at the fundus in 12 cases. It was implanted in the cornua 5 times. There were 10 cases of placenta previa in this group. The whole interior of the uterus was covered 6 times, as it was once in our series. There were 5 cases of diverticulum, one in a primipara, which points to this being of congenital origin. In a museum specimen, it was found implanted in the cornu and septum of a bicornuate uterus.

DR. HARER (closing).—The only thing I would add is that in these cases, the point of rupture of the membranes was noted in each case. This information is available from these 1,000 cases but was not included in the paper.

Passalacqua, N.: The Influence of Ovarian, Mammary, Placental, Pituitary and Suprarenal Extracts Upon the Hematopoietic Organs and the Blood, Monitove ostet-ginec (Bologna) **8**: 18, 1936.

The author considers and briefly reviews the principles of the uteroovarian cycle according to Sfameni, which regulate almost all the functional manifestations of every single organ or organ group in woman during her sexual period of life, during menstruation as well as during pregnancy. From his studies he concludes that the hormonal secretions of single glands or groups of glands of internal secretion, under certain circumstances, also can influence the hematopoietic organs and blood constitution.

AUGUST F. DARO.

A BACTERIOLOGIC STUDY OF 500 CONSECUTIVE ABORTIONS, WITH TREATMENT AND RESULTS*

T. K. Brown, B.S., M.S., M.D., and George A. Hunt, B.S., M.S., Ph.D.,
St. Louis, Mo.

(From the Department of Obstetrics and Gynecology, Washington University School of Medicine and the St. Louis City Hospital)

THE purpose of this study is to emphasize the importance of the group of organisms, known as anaerobes, in 500 consecutive cases of abortion. Treatment and results will also be discussed.

Krönig[1] recognized and described anaerobic streptococci in 1895. In 1905, Little[2] reported a case of puerperal infection due to anaerobic streptococci occurring in the service of Dr. Whitridge Williams. The importance of this group of organisms was not recognized until Schottmüller[3] reported, in 1910, a series of twenty-five cases with a 50 per cent mortality. He stated that the anaerobic streptococcus is a virulent pathogenic organism and cannot be regarded as a parasite, because once having invaded the tissues, thrombi or blood stream, it has pathologic properties. Schwarz and Dieckmann[4] reported forty-two uterine cultures in 1925 and corroborated the findings of Schottmüller. In an attempt to show the probable source of the anaerobic organisms, Soule and Brown[5] (1932) studied the vaginal flora of normal clinic patients during pregnancy and found anaerobic growth in 60 per cent of the cases. These studies were continued and in 1934, Schwarz and Brown[6] reported an incidence of 83.3 per cent anaerobic organisms in 228 cases of puerperal infection treated in the previous ten years on the Obstetrical Service of the Washington University School of Medicine.

It seemed desirable to study another group of cases and compare results. Such a study has been accomplished on the Gynecological Service of the St. Louis City Hospital, No. 1 (for white patients), in a period of eighteen months (500 cases). The treatment of the patients has been carried out under the direction of the Resident Gynecologist, and the bacteriology has been determined by the Bacteriology Laboratory of the hospital.

Cases with positive uterine cultures were divided into three groups: (1) Aerobic, showing only aerobic growth. (2) Mixed,† showing both aerobic and anaerobic growth. (3) Anaerobic, showing only anaerobic growth. Table I shows the incidence of positive cultures and then stresses the predominance of the anaerobic group of organisms.

Table II gives some idea as to the types of abortion encountered. If the doubtful group is considered as probably induced (although not admitted as such), we find that over half of the abortions in this series are likely induced.

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*Read, by invitation, at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25 to 27, 1936.

†Included in the "mixed" cultures are the cases in which the facultative anaerobes were demonstrated. This was done intentionally, in order to simplify the bacteriological study so that it could easily be applied in a clinical way.

Table III combines the findings in Tables I and II and indicates the relatively high percentage of negative cultures in spontaneous abortions. The very high percentage of anaerobic growth in the cases with positive cultures in all types of abortions is illustrated.

Table IV shows the very low incidence of positive blood cultures and analyzes them according to the types of uterine cultures. It will be noted that one case with an anaerobic uterine culture was found to have a blood culture which showed the presence of *B. typhosus* and the patient was immediately transferred to the Isolation Hospital.

TABLE I. UTERINE CULTURES

	CASES	%
Negative	200	40.0
Positive	300	60.0
Total	500	100.0

Analysis of 300 Positive Uterine Cultures

	CASES	%	COMBINED TOTALS CASES	%
Aerobic	24	8.0	160	53.3
Mixed { Aerobic / Anaerobic }	136	45.3		
Anaerobic	140	46.6	276	92.0

TABLE II. TYPE OF ABORTION

Induced	36.6%	55.6%
Doubtful	19.0%	
Spontaneous	43.8%	44.4%
Stem pessary	0.6%	
Total of all cases	100%	

TABLE III. ANALYSIS OF UTERINE CULTURES

TYPE OF ABORTION	NEGATIVE	AEROBIC	MIXED	ANAEROBIC	TOTAL CASES	TOTAL ANAEROBES
Induced	56 (30.6%)	10 (5.4%)	69 (37.7%)	48 (26.2%)	183	92.1%
Doubtful	29 (30.5%)	6 (6.3%)	29 (30.5%)	31 (32.6%)	95	90.9%
Spontaneous	115 (52.5%)	8 (3.6%)	37 (16.8%)	59 (26.9%)	219	92.3%
Pessaries (stem)	0	0	1 (33.3%)	2 (66.6%)	3	100%
Total	200	24	136	140	500	

TABLE IV. BLOOD CULTURES

Uterine Cultures		
Negative	0	
Aerobic	1	
Mixed	6	
Anaerobic	1	(Typhoid fever)
Total	8	

Table V gives the analysis of aerobic organisms obtained in the aerobic and mixed groups of uterine cultures. Considerable emphasis is given to the rôle played by the various types of staphylococci as frequent uterine contaminants.

TABLE V. ANALYSIS OF AEROBIC CULTURES

	AEROBIC GROUP	MIXED GROUP	
B. coli	2	30	
Staphylococcus (unidentified)	0	29	
Staphylococcus albus	5	15	54
Staphylococcus aureus	5	10	
Sporeforming bacillus	7	14	
Diphtheroids	0	12	
Nonhemolytic streptococcus	1	11	
Hemolytic streptococcus	2 (2 died)	7 (2 died)	
Streptococcus viridans	0	0	
Diplococcus (unidentified)	0	2	
Gonococcus	0	2	
Yeast	0	1	
Not classified	2	3	
Total	24	136	

TABLE VI. HOSPITALIZATION AFTER TREATMENT

UTERINE CULTURES	CASES	AVERAGE DAYS
Negative	200	5.8
Aerobic	24	5.5
Anaerobic	140	6.6
Mixed	136	7.4
Total	500	6.3

TABLE VII. DIAGNOSIS AND TREATMENT OF PUERPERAL INFECTION

1. Differential diagnosis.
2. Preparation of patient: do not catheterize because of danger of urinary infection.
3. Intrauterine culture and examination of patient.
4. Emptying of the uterine cavity of débris with patient in seminarcosis, but *without* anesthesia by:
   a. Foerster's sponge-holding forceps.
   b. Uterine wiper.
5. Intrauterine douche with $KMnO_4$ (1-1,000) at 110° to 115° F., under 15 cm. of water pressure or less (irrigating can resting on symphysis), using a large size Bozeman intrauterine douche *cannula*.
6. Administer ergot preparation, but avoid pituitary preparations.
7. Follow-up treatment:

   Semi-Fowler position.
   Ice-bag to lower abdomen.
   Ergot preparations.
   Rapidly increasing diet (if no peritonitis).
   Low pressure vaginal douches, $KMnO_4$ (1-1,000) beginning the third day.
   Start getting up on fourth or fifth day.
   Transfuse for anemia.

   In cases with signs of peritoneal irritation:

   Nothing by mouth.
   Intravenous glucose.
   Subcutaneous saline.
   Transfusions, large and frequent.
   Wangenstein apparatus.
   No laxatives.
   Daily tap water enema.
8. If temperature remains elevated reexamine every second or third day to determine presence of pelvic thrombophlebitis or beginning pelvic abscess formation.
9. Patient discharged at end of one week under conservative instructions.
10. Reexamine in two or three weeks.

Next in frequency is the *Bacillus coli*. The incidence of the *Streptococcus hemolyticus* is very low, but when it is the offender, the mortality rate is high. In two cases the gonococcus was cultured as the offending organism.

Table VI illustrates the very short period of hospitalization required after treatment. This point is of great interest both to patients and the hospital administration.

TREATMENT

The treatment of puerperal infection has been divided into (1) conservative and (2) active. It appears that the conservative method would be an active method of treatment as has been used in this series of cases. In other words, the inactive treatment is not always conservative, because it may permit the spread of a local infection.

When a patient in the puerperal state develops signs of infection, which cannot be accounted for after the usual diagnostic methods have been used to rule out all other possible infections, then it seems justifiable to investigate the uterine cavity.

The surgical principles involved in the treatment of this series of cases are (1) drainage of an infected wound site and (2) débridement of a potentially infected cavity. This is done with a minimal amount of manipulation in order that further trauma may be avoided. We have demonstrated that this procedure can be safely performed by a junior interne under proper supervision. A general anesthetic is not to be used, because this would remove the inhibiting influence of the patient's response to pain which is usually indicative of too active manipulation. The patient should be under the influence of some sedative so as not to be too apprehensive. Morphia (1/6 gr.) with hyoscine hydrobromide (0.0005 gm.) followed by hyoscine (0.0005) in forty-five minutes are given so that the second dose is given at least thirty minutes before the patient is prepared for examination.

The perineum is prepared with 5 per cent neutral acriflavin in 10 per cent acetone and 50 per cent ethyl alcohol. The bladder is *not* catheterized because of the danger of contamination which may frequently superimpose a urinary infection. Drapes are placed. A Graves' vaginal speculum is used to obtain exposure of the cervix. If this is not satisfactory, large vaginal retractors will be necessary. The vagina and cervix are then prepared with the above solution of 5 per cent neutral acriflavin. Treat the cervical canal with this solution, then dry carefully with sterile gauze. A culture is then obtained from the uterine cavity with a modified Little tube. If it is not possible to have careful bacteriologic investigation of the material obtained, at least several smears of the material can be made and stained by the Gram method. This has been done routinely and found to check very well with the bacteriologic findings. Both aerobic and anaerobic blood agar slants should be made. The Wright anaerobic technic is used in search for anaerobic organisms.

After the culture has been obtained, a gentle bimanual examination is done to determine evidence of any spread of the uterine infection, pelvic abscess or thrombophlebitis. This is also done without an anesthetic in order that the patient's reaction to pain will limit the extent of the examination. Too much pressure will not be used, which might cause rupture of an abscess internally. The uterine cavity is very carefully investigated with a Foerster's sponge-holding forceps, plain jaw. Dilatation of the cervix is usually sufficient to permit this. The sponge forceps is inserted closed to the depth desired, opened, closed, and removed to see

if any tissue has fallen within the jaws. The forceps should not be advanced with the jaws open, because of the danger of grasping the uterine muscle. The uterine wall is next explored very systematically and with great gentleness by means of a "uterine wiper" (formerly called a vaginal depressor) much as a windshield wiper wipes the surface of the windshield, without marring the surface. (NO curettage is done.)

The uterus is usually found to be relaxed in such cases. After mechanical removal of any retained débris, the patient is given an intrauterine douche using a Bozeman's extra large intrauterine douche nozzle. This instrument permits the free exit of the solution from the uterine cavity without any pressure being established. Two liters of a 1:1000 solution of potassium permanganate in sterile water at 105° to 110° F. are used. This solution is usually acidulated with 50 c.c. N/1 sulphuric acid. The bottom of the douche can is held at the level of the symphysis so that the water pressure of the solution as it enters the douche nozzle is 15 cm. or less. Such a douche results in (1) removal of small bits of tissue remaining after mechanical emptying of the cavity, (2) firm contraction of the uterus, including the cervix, so that bleeding is controlled and the sinuses are closed, (3) elimination of the putrid discharge which is characteristic of the anaerobic infections.

Table VII outlines the treatment and postoperative care.

We agree with Schottmüller that the manner of spread of such contamination is by way of the endometrium; the organisms invade the uterine wall, parametrium, and thrombosed veins. Therefore, the earlier the local endometritis is treated, the more prompt is the cure. Less complications develop and the period of convalescence is much shortened. The possibility of future sterility is greatly lessened as evidenced by patients returning shortly with another abortion and others presenting themselves for delivery at term. The thrombosed veins in contradistinction to the circulating blood offer a fine culture medium. The proliferating organisms desire hemoglobin as their food and low oxygen tension in their environment. These organisms usually have a definite proteolytic tendency and are able to disintegrate thrombi so that small particles break off and gain access to the blood stream and other organs, particularly the lungs.

TABLE VIII. MORTALITY

TOTAL CASES	TOTAL DEATHS	PERCENTAGE
500	7	1.4

Six of these cases had serious inflammatory complications upon admission and the seventh was almost exsanguinated.

TYPES OF UTERINE INFECTION		BACTERIOLOGY OF FATAL CASES		
Aerobic	2	*Staphylococcus aureus*	1	14.2%
Mixed	4	Anaerobic streptococcus	2	28.5%
Anaerobic	1	Hemolytic streptococcus	4	57.1%
	7		7	

The *Streptococcus hemolyticus* was cultured from the uterus in 9 instances among this series of 500 cases—an incidence of 1.8 per cent. Only 4 of those cases terminated fatally—a mortality of 44.4 per cent.

The proteolytic properties of anaerobic streptococci probably are responsible for the marked loss of hemoglobin in patients with this type of infection. Therefore, one is able to see the rationale of large and frequent blood transfusions in the treatment in such cases. Since treatment has been instituted at an earlier time in the course of the infection, the demand for transfusions has greatly diminished. The

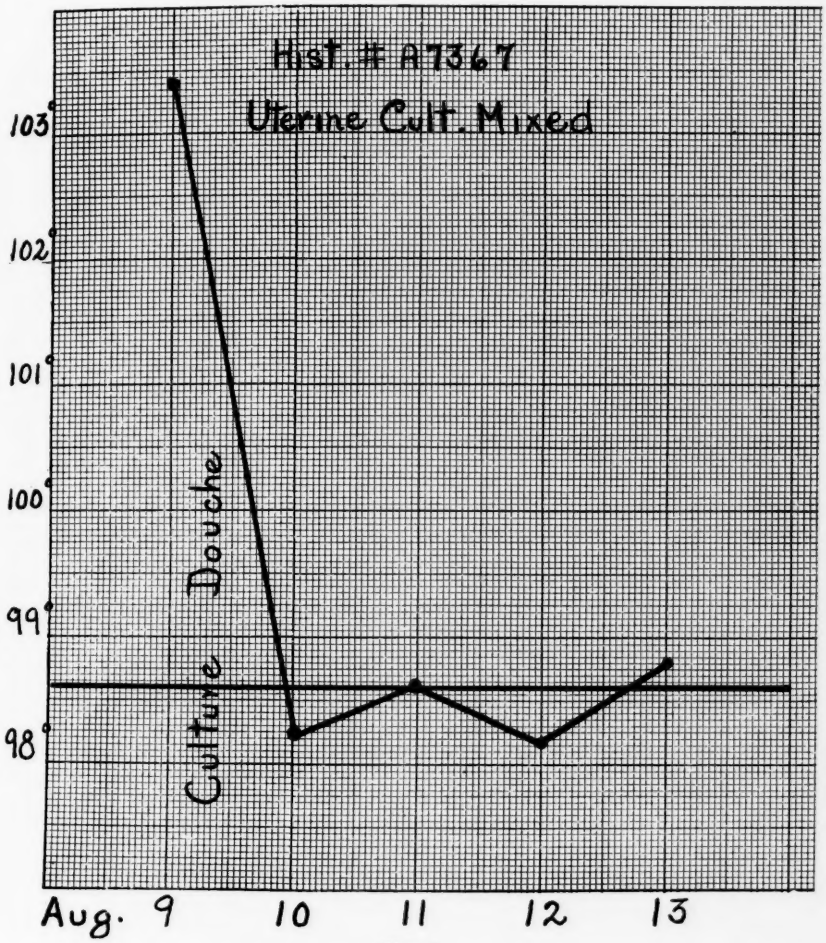

Fig. 1.

disease seldom runs the prolonged or chronic course formerly expected. Leucopenia is a common finding in cases of puerperal infection which are uncomplicated.

RESULTS

Fig. 1 illustrates a typical temperature chart, with the prompt return to normal after treatment.

Table VIII outlines the mortality figures and we observe the hopelessness at the time of admission of the patients who died. The cases are analyzed as to type

TABLE IX. DEATHS

HISTORY	TYPE OF ABORTION	BLOOD CULTURE	COMPLICATION	TRANSFUSIONS	TYPE OF INFECTION	CAUSE OF DEATH (CHECKED BY AUTOPSY)
F. H. 11653 32 days	Criminal (Midwife)	Neg.	Pelvic abscess	8	Anaerobic (Anaerobic Strep.)	Peritonitis Multiple lung abscesses
P. C. 14344 1 day	Self-induced (Catheter 30 da.)	Pos.	Septicemia	0	Mixed (*Staph. aureus*)	Septicemia
E. S. 17104 24 days	Criminal (Midwife)	Pos.	Peritonitis septicemia	4	Mixed (Hemolytic Strep.)	Septicemia Peritonitis Lung abscess, Lt.
N. J. 19808 12 days	Self-induced (Catheter)	Neg.	Exsanguinated	2	Aerobic (Hemolytic Strep.)	Peritonitis Multiple lung abscesses
D. W. A-4031 3 days	Self-induced (Medicine dropper)	Pos.	Peritonitis septicemia	2	Mixed (Hemolytic Strep.)	Peritonitis Septicemia
S. G. A-10239 13 days	Criminal (Midwife)	Pos.	Peritonitis	4	Mixed (Anaerobic Strep.)	Peritonitis Perforation of uterus
N. S. A-17168 8 days	Self-induced (Catheter)	Pos.	Septicemia	3	Aerobic (Hemolytic Strep.)	Septicemia Early pneumonia

of uterine infection and also as to the predominant organism. The relative unimportance of the *Streptococcus hemolyticus* as to morbidity is stressed, and then its great importance as to mortality is emphasized. The situation in this particular type of infection is by no means hopeless and treatment should be similar in all types of cases, irrespective of bacteriologic findings.

Table IX analyzes the fatal cases, showing the hospital days and other important findings. Autopsy was obtained in every instance to check the cause of death.

CONCLUSIONS

1. Anaerobic organisms play a predominant rôle in the bacterial contamination of the uterine cavity following abortion as they are shown to be present in 92 per cent of the patients with positive cultures in this series of 500 consecutive cases.

2. This finding has been obtained by a different group of clinical assistants aided by another laboratory corps, but checks very closely with the findings of the Department of Obstetrics and Gynecology of Washington University School of Medicine.

3. Sixty per cent of uterine cultures are positive.

4. The incidence of *Streptococcus hemolyticus* as the infecting organism was very low (1.8 per cent), but its importance as a factor in mortality (57.1 per cent) must not be overlooked.

5. The small number of positive blood cultures should indicate its minor importance as a diagnostic sign. It means much more as to prognosis.

6. The period of hospitalization is very short, average 6.3 days after treatment.

7. Treatment should be early and active—culture, gentle evacuation of the uterine cavity, followed by an intrauterine douche.

8. Cases coming to fatal termination were moribund upon admission.

(I wish to express my thanks to the Resident Staff of St. Louis City Hospital, No. 1, for their excellent cooperation.)

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630 South Kingshighway Boulevard

DISCUSSION

DR. WILLIAM J. DIECKMANN, Chicago, Ill.—In evaluating the management of abortion cases we have always considered only the mortality. In his closing remarks I hope Dr. Brown will say something about the follow-up of these cases with reference to subsequent sterility, incapacity, subsequent abortions, and ectopic pregnancy as a result of the infection, and something about fibrotic uteri that may develop due to the subinvolution.

The importance of anaerobic streptococci is shown by his report. Whenever uterine cultures are grown both aerobically and anaerobically, it is noted, usually with surprise, that the majority of the organisms are obligate anaerobes. At the Queen Charlotte's Isolation Hospital, where some of the best research work on puerperal infection is being done, about one-third of the infecting organisms are anaerobic streptococci. At the Chicago Lying-In Hospital, our incidence of abortions is small, but it is interesting that in a group of 25 cases of postabortal and puerperal infections, ten or 40 per cent were due to anaerobic streptococci. In 70 uterine cultures, 40 per cent were anaerobic streptococci, 14 per cent mixed and, a very interesting thing, only 6 per cent hemolytic streptococci.

In the subsequent discussion, I hope that the question of radical versus conservative treatment will not be introduced. What Dr. Brown has done is not radical. Adair and Davis in their work on the ergot preparations have introduced bags into the uterus in more than 300 patients with no patient having a temperature of 38° for longer than twenty-four hours. Koff at Johns Hopkins introduced a bag in 70 cases with only one patient developing subsequent puerperal infection. The uterus can be invaded without danger, if proper technic is used.

I think it is of importance to know what type of organism is present, and particularly with the anaerobic streptococci to remove the fragments of placenta that are left. It is not a curettage that Dr. Brown has advised. The purpose of the douche is to stimulate the uterus to contract. There is no hope of washing out the bacteria.

DR. OTTO H. SCHWARZ, ST. LOUIS, MO.—Various maternal mortality reports have stated that the number of deaths from puerperal infections was entirely too great and that the cause of these deaths was entirely due to neglect. I have maintained that such a sweeping statement was a mistake, because anerobic infection would occur in many cases whether or not the patient was contaminated.

Puerperal infections are due to two types of organisms, those harbored by the patient and those that are introduced. The anerobic are the chief cause of the endogenous infections. They can develop under certain conditions and can cause all the conditions of pathogenicity, and our problem today as obstetricians is not so much in preventing the exogenous infections by good technic as in preventing these endogenous infections. Nevertheless our problem is still twofold, the endogenous and the exogenous infections. Of course, with bad technic the exogenous prevail, but with good technic it is the endogenous infections that we must bear in mind. When we do as Dr. Brown has done we shall see fewer cases of puerperal infection in well-regulated maternity hospitals.

DR. BROWN (closing).—That the infection is favored by inadequate drainage is demonstrated very thoroughly in the many cases that we have had. If we can establish drainage, get the blood clots out of the cervical canal and empty the uterus, the patient responds very quickly with a normal temperature and no complications develop.

We have had no serious complications in these 500 patients treated by this method. We have had patients come back after several months with subsequent abortions, and quite a number of patients return within a year for delivery. We do try to educate the patient against the use of abortion, not by preaching but by trying to show the dangers. Many of them come back for subsequent delivery, which I think is of some aid in the lowering of maternal mortality.

Subsequent examination shows the pelvis to be absolutely negative without masses, tenderness, or induration, and the menstrual cycle returns to normal. Since the early

treatment of these patients, thrombophlebitis is almost unheard of. The patient either comes in with it already developed or she does not get it.

Transfusions have been diminished in number tremendously since active treatment. The patient immediately improves, and she regenerates her blood very quickly as soon as the infection and bleeding are arrested.

We do not do a curettage. We empty the uterus and wipe very, very gently. I do not believe in wiping with the fingers because in doing so it is necessary to push the uterus down in order to reach it and get the finger in. In doing this you will squeeze the uterus as a sponge and disseminate the infection.

SIMILARITY IN CERVIX OF RHESUS MONKEY AND WOMAN*

ROBERT L. DICKINSON, M.D., F.A.C.S., NEW YORK, N. Y., AND
CARL G. HARTMAN, M.A., PH.D., BALTIMORE, MD.

(From National Committee on Maternal Health, Inc., and Carnegie Institution of Washington)

TO JUDGE by thirty adults in the colony of the Carnegie Institution in Baltimore, examined March 6, 1935, the difference in form and pathologic behavior between the vaginal portion of the cervix of the macaque and that of woman is almost altogether one of size, a matter of four-tenths in diameter. Hence, in this field biology and gynecology may find teamwork profitable.

To permit easy visual comparison, drawings to scale were made by one of us (D.). These have been set over against examples in women, each opposite a human cervix which, by employing the above average, is scaled down to that of the monkey. The human types were selected from more than a thousand sketches in the office records of the senior author of this report. These cervix drawings had been made from life, usually life-size, duly checked by measurement, and often in color. This habit developed because of the experience of fifty years that much time could be saved by making life-size sketches as compared with writing entries. By visualized comparison, the similarity is here shown to be astonishingly exact, so much so that, in the accompanying figures, one will not be able to tell which is which save in four instances. The *human and the simian portio vaginalis will be seen to agree in conformation and invagination, laceration and inflammation, eversion and erosion, secretion and vascularity, infantilism and asymmetry.* Cystic degeneration and polyp, cancer and certain infections alone were missing in this short series.

Three differences appear. These are:

1. Facile dilatability of the untorn lower cervical canal and of each external os, a condition almost unknown in women.

*Read at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25 to 27, 1936.

2. Corrugation of the surface in several instances, with the vaginal rugae covering the anterior lip, or both lips, quite to the external os, a very rare finding in women.

3. Adhesion of the seminal plug to a circular rim of the most projecting part of the portio, not seen in women (Fig. A, 1, 2, 3).

The vagina is worthy of detailed study. It was noted that in 22 instances there was a range from relaxed walls, quite smooth, in a third (C 2, 235), through fine laid rugae in another third (C 2, 73) up to a striking kind of pointed, rigid, almost rasplike points and ridges, in the remainder (C 2, 2). Some walls were very inelastic. As in women, the anterior wall had more corrugated surfaces than the posterior and the lower more than the deeper section. The posterior fornix was deep in an animal one would suspect of vigorous attention from a well-built male, if one drew an inference from the human female.

There is a range of color from white (4 cases), even chalky white, through pallid (1) grayish (1) to faint pink (5). This marked lack of color is hardly seen in women. One was purplish, the "erotic" human type, with smooth vagina, prominent clitoris and large wrinkled prepuce.

CLITORIS

The clitoris of this and other monkeys calls for drawings of larger size, with indication of scale and with detail not given in the literature, even in that of Bolk and Pocock. It is noteworthy that in our few macaques there is exhibited more range of variability in this organ than has been shown in the human beings in the Dickinson Atlas, which exhibits far the largest variety in shape and size in vulvas, yet published, and includes a series of measurements and drawings of the clitoris. As in women, so in the rhesus monkey, there is a wide divergence in dimensions of the clitoris, in location, in axis, in alterations in axis during erection, in erectability, in the location of the prepuce and the amount of preputial corrugation, the latter raising the question of persisting digital frictions in rhesus (E 3, 4). The special traits were a pigmentation not seen in women, blackish, bluish, or purplish; a prepuce far up the shaft, and a relatively much greater projection, resembling a miniature stubby penis or the intersex organ of the human being. In this observation the clitoris was not regularly measured or drawn, but a sample is shown in E 3, where, in the same bracket, a comparison is made with the organ of other monkeys which Dickinson sketched in the Yerkes group at New Haven.

The clitoris of the little spider monkey (Bolk '07, 307) shows the same size (6.5 cm.) and same slit as the intersex clitoris of the woman who lived as a male dock porter, shown in the Dickinson Atlas, Fig. 117. The Ateles monkey, however, lacks erectile tissue in its huge clitoris.

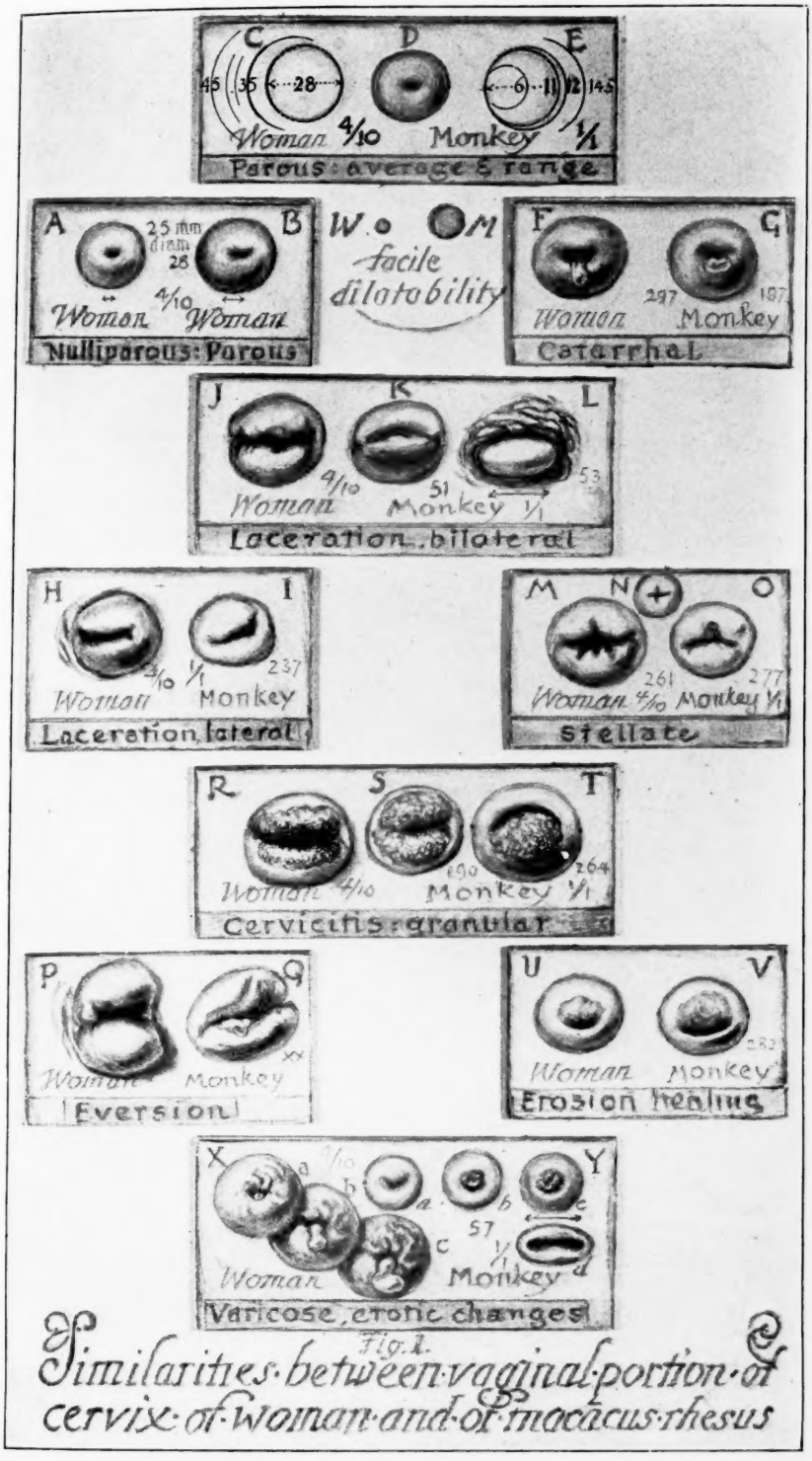
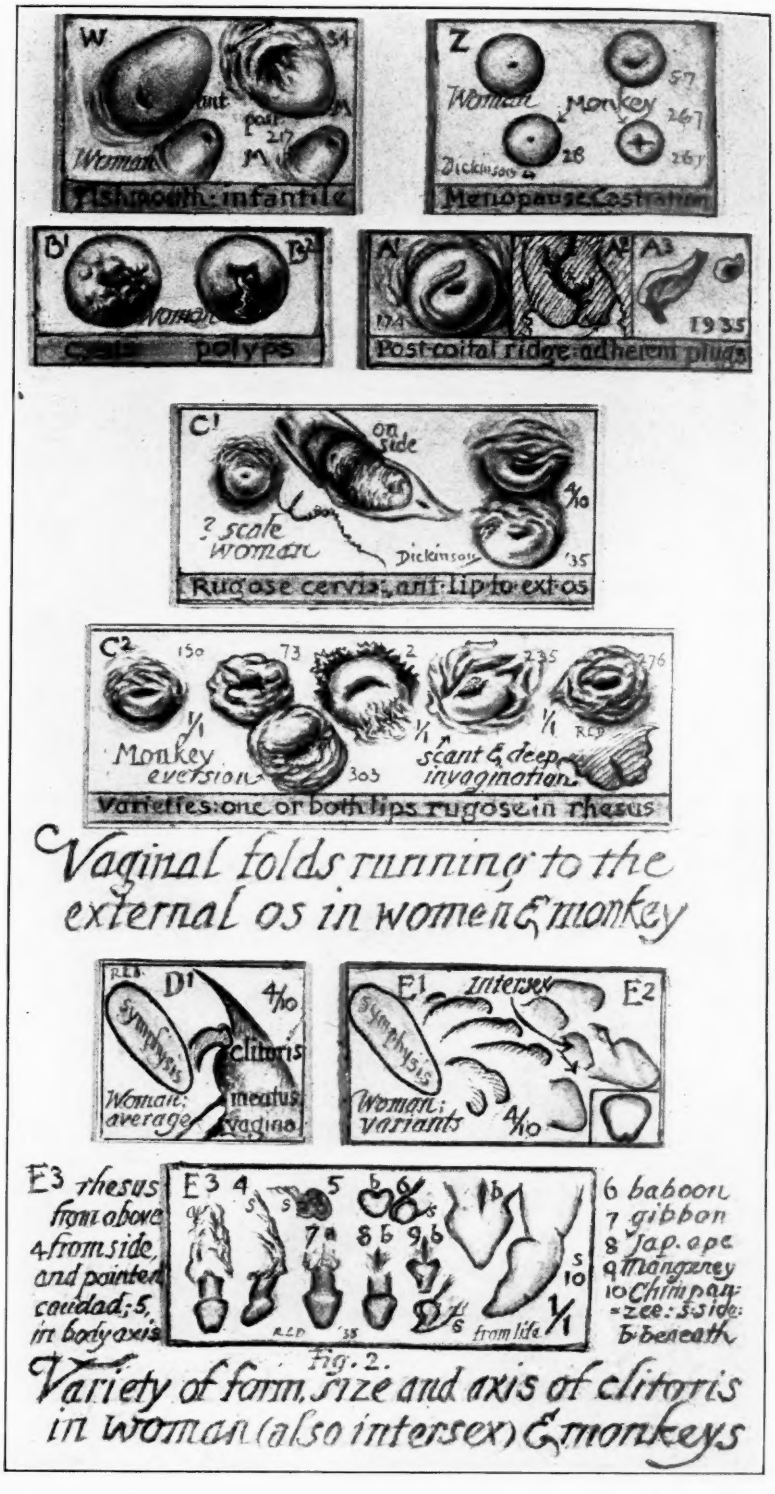


Fig. 1.

Similarities between vaginal portion of cervix of woman and of macacus rhesus


W
Woman
Fishmouth: infantile
Z
Woman
Monkey
Menopause Castration
B1
B2
polyps
A1
A2
A3
1935
Post-coital ridge: adherent plugs
C1
on side
? scale woman
Dickinson
Rugose cervix, ant. lip to ext. os
C2
Monkey eversion
scant & deep invagination
Varieties: one or both lips rugose in rhesus
Vaginal folds running to the external os in women & monkey
D1
symphysis
clitoris
meatus
vagina
Woman: average
E1
Intersex
E2
symphysis
Woman: variants
E3 rhesus from above 4 from side, and pointed caudad; 5, in body axis
6 baboon
7 gibbon
8 Jap. ape
9 mangabey
10 Chimpanzee: S side: b beneath
from life
Fig. 2.
Variety of form, size and axis of clitoris in woman (also intersex) & monkeys

CERVIX

For the cervix there were 27 monkeys on which the part could be conveniently measured and depicted. There were 8 of the type typical of the parous woman, namely with a small transverse slit (Figs. B, D, F). Except when torn, anterior and posterior lips were about equal in anteroposterior diameter. Then there were 9 with considerable lacerations, showing all of the human varieties, unilateral, bilateral, stellate and crescentic, the convexity of the latter either caudad or ventrad, and there were tears running out to the vaginal wall (Figs. H to V). Eversion ran true to familiar human types. Cervicitis was again an interesting miniature, ranging from mere mucus catarrh or marked redness, mainly of the slightly everted canal, to granular erosion bleeding at a touch, the lip or lips involved being swollen and outrolled (G, S, T, V, C 2, 303). There was in one sterile animal a conical cervix with pinhole os (and a relatively narrow corpus which did not undergo the monthly cycle of broadening, Wislocki 1932, 217) resembling arrest of development as found in the clinic. Here also was seen our familiar picture of the dwindled portio of age, a year after the animal's castration, or after cessation of ovulation. One cervix was rigid and undilatable as in women (Z 28); one dilatable its full diameter (Fig. Y, *d*). There was not even missing what Dickinson calls the erotic cervix, with prominent veins and outpouring mucus, changing in vascularity, size and hue, becoming dusky as one watches (Y, *a*, *b*, *c*). The illustrations will show better than words the wide variety in the clinical evidence of childbirth and of rate of involution, possibly of sex excitement.

The average external diameter in this group was a little over 11 mm. The eight healthy cervices of parous animals plus the six wrinkled cervices, adding those torn but not thickened, 19 in all, averaged 11 mm. (Fig. E). The comparative range in diameter was somewhat less than among women (Figs. E and C). (Reporting 3 specimens, Wislocki, '32, 171, gives for the whole uterus, 40 mm. length; 18 mm. breadth; 14 mm. thickness, and for the cervix 16 by 12 mm., 16 by 8 mm., and 15 by 10 mm.)

There were five injured or inflamed cervices running to 14 or 15 mm., and three sterile or atrophic anatomies of 5.5 to 6 mm. (Figs. E, W, Z).

Laceration was evident among the twenty-two monkeys known or thought to have delivered babies, being definite or pronounced in nearly one-half of these. Cervicitis was present in one-fifth of the fully developed organs; with three striking examples of large areas of roughened redness, two being shown in S, T. Rugose or plicated surfaces on the portio occurred in more than one-fifth (C 2), completely covering the area from vaginal wall to external os in three. Invagi-

nation was noted as slight or absent in five cases, and this defect was sometimes accompanied by a wrinkled surface.

Dilatability was noteworthy. Gentle testing showed, among eleven untorn cervices, on the average, a distensibility equal to half the outside diameter (underneath Fig. D, also Y). This is more than double the relative capacity of the human cervix, even where the powerful leverage of the branched dilator or the push of graduated tapering dilators is brought into play. It is as if the undamaged human canal would, with slight pressure, admit the average male little finger. Of these eleven canals three could be easily opened to 8 mm. and one to 6 mm., or as if the unlacerated, fully involuted cervix of a nonpregnant woman allowed the thumb to pass. Indeed one monkey cervix of 8 mm. external diameter permitted an 8 mm. passage (Fig. Y, *d*) and two of 8 mm. dilatation were in cervices of 10 and 11 mm. outer diameter. If women were like this, emptying the uterus in early pregnancy by passing a finger would be simple, whereas it is not feasible without damage or incision. Abortion, by separating the ovum from the uterine wall with a (sterile) finger nail as curette, guided by the sensitive finger tip, would be too easy.

The corrugated cervix, or rugose portio vaginalis, shows part or all of the surface looking like vaginal wall, but usually with distinct rounded projection into the vault of the vagina. It suggests an incomplete process of invagination, or smooth-stretching of the epithelial covering, or else arrest of development. In human fetal development and in childhood this ridged surface may be detected (Bayer). The rugae were transverse or crescentic in all but one of the seven, and on both lips in three. In one the folds pointed to the os.

Wislocki says (1932, 174) of the rhesus monkey "the orifice is situated near the ventral border of the cervix so that the dorsal lip is approximately twice as thick as the ventral one. . . . The vagina is lined by coarse longitudinal rugae covered by a multitude of delicate transverse plicae. In the fornix the plicae become longitudinal and extend into the cervix, much more pronounced, however, on the small, ventral lip than on the dorsal lip, which in some specimens is nearly smooth. The plicae converge toward the external os which they enter" (Sic). His gorilla, shown in Broedel's beautiful drawings, presents a cervix which looks a bit like C 2, 2. Wislocki declares (175) that the cervix "is an extremely variable structure in the Simiae, occurring in the catarrhine and platyrrhine (American monkey), at times in even more differentiated form than in the anthropoids and men." Dickinson draws attention to the fact that in the older museum specimens of the cervix, vagina, or vulva, and even in the large and remarkable Hoffman-Haberda Vienna medicolegal exhibit of external genitals, the surfaces are puckered and therefore distorted. This is particularly true of the Bischoff lithographs with their generally corrugated surfaces as compared with Dickinson's long published series drawn from life, his unpublished drawings and the Heitzmann lithographs of the cervix.

Wislocki (1932, 174) describes the rugae of the cervix of various monkeys as well as the degree of invagination. In the spider monkey, the cervix is large and prominent, with radiating rugae. In the capucine, the howling monkey and the Titi monkey, it is provided with rough excrescences; in the marmoset with an orifice

delicately fimbriated. The gibbon and the night monkey show "no circumvallation, the cervix passing unsignalled into the cervix (meaning vagina?) as a funnel shaped passage, the lips of which are thrown into delicate longitudinal leaflets or fimbriae."

In our 27 monkeys there were seven instances of rugose portio, ranging from small areas to complete coverage (Figs. 1, L, and C, 2). In women only three drawings of such findings are found, so far, by Dickinson, among routine sketch records of the cervix, among his nearly 5,000 retained office histories (Fig. 2, C, 1). No rugose cervix occurs in the only considerable and important published collection of pictures of the cervix, the Heitzmann lithographs in color, 113 in number. Jayle's series has missed this also, among his 33 shrewd observations, unless his Fig. 299, page 501, on a woman of twenty-four, which he calls atrophy, is defective development with its smooth anterior lip, or Fig. 296, page 499, first seen at thirty-five, with no invagination and no projection, as in the monkeys. W. T. Kennedy and J. W. Davies of New York each observed a patient with this conformation after Dickinson had posted a drawing on the bulletin board of the Woman's Hospital.

The cervicitis shows the same range as in women, with like outrolling and swelling, and the mate of the rather frequent type where, after crescentic injury, one lip is larger than the other and alone eroded (Figs. T, V), it being either anterior or posterior. Even a cyst high up the canal is reported in the gorilla (Wislocki, 1932). In Case XX (Fig. Q) we see subinvolution, where there was voluminous discharge of clear mucus noted. The fertility of rhesus in captivity (35 per cent) might be raised by curing the cervicitis. From rhesus, the gynecologist could well develop clues or tests from the relation of cervicitis to sterility or to general health, to ovulation in particular and to stages of the cycle; with the bacteriology of cervicitis in the monkey; and results from various treatments.

Joachimovitz shows some fine sections of the cervix and corpus.

MEATUS

The meatus might be of importance to gynecology because of the rebellious infections found there in women and the need of experiment in animals. Jayle (1918) and Dickinson (1904, 1933) have pictured its form, but the former ignores, on page 407 and elsewhere, the meatus glands, while at the same time proving the best of sources anent location and number of the vestibular glands.

Wislocki found in rhesus at the meatus urinarius two papillary folds, and in a guenon monkey, slight folds guarding the meatus, none in the anthropoid. He denies them to women (194). I (D.) have pictured and described the frequency in woman, also a monkey or fetal type of urethral opening almost or quite on the vaginal wall (1933). Jayle

shows the rounded projection of the meatus in women, resembling that of some monkeys—a condition of which the student of monkeys seems unaware.

The illustrations in very many of the Simian reports are on such a small scale that the cervix is hard to study. The general absence of indications of scale is notable and surprising. Wislocki is careful in this matter and specific beyond other authors concerning the surfaces of the cervix and vagina (1932, 173, 175) and appreciates the variants that may occur within a given species.

As a clinician, the interest of the gynecologist in these animals leans toward practical considerations rather than toward comparative anatomy. Here the size, cheapness, readiness of domestication and relative fertility of a given animal count heavily in matters of research looking toward improvements in human diagnosis and treatment. The rhesus meets most of our needs, except for the flap (Klappe) closing the canal, and rendering the cavity of the body of the uterus inaccessible, save, apparently, at certain times. I found very marked differences in depth of penetration when trying to test the dilatability of the cervical canal with a forceps, with the tips closed when passed, then spread as wide as the blades would open easily.

CERVICAL CANAL

The cervical canal of the rhesus monkey shows an extraordinary sigmoid sweep, the "two nearly right angled turns" of Wislocki. This "flap" (or Klappe) is shown in A 2. There are two pockets, or more, according to Joachimovitz (1928, 531, 470). He says this deflection is perhaps a stage of the cycle, accompanied as it is by increase of mucus and enlargement of glands, and has clearly pictured the condition. He declares that this transverse fold may stand out in women, particularly in infantile and old uteri. He observed two women with it in adult life and calls it "an infantile stigma." Certainly the gynecologists of the eighties who probed the cavity of the uterus in every case found canals refusing to allow the sound to pass where previously it had slid in easily. I (D.) accounted for this by spasm with tenderness at the internal os in some cases, by large new high cysts in others (Atlas Fig. 34), by inflammatory swelling in others. Yet there were cases inexplicable, which a variable transverse fold would have accounted for. This condition must not be confused with anteflexion, nor with the postmortem slump and crook common in the frozen sections (Atlas Fig. 21). It does, however, handicap our use of rhesus for biopsy of the cavity of the body where it blockades entry.

The comparisons made above, though few and sketchy, suggest new tests, on these eroded surfaces, by implantation of some virulent strain

of gonococcus, because research and treatment of that unconquered scourge, gonorrhea, is gravely handicapped for lack of an experimental animal. The other human habitat of the Neisser germ, the pair of glands at each side of the urinary meatus, might be searched for and injected, if found in the rhesus monkey. A pair of glandular openings are found on each side of the meatus in the gorilla by Wislocki (1932, Plate II, C).

The form of the speculum, not Sims, but simian, for the purpose of examination of the cervix and vagina, may be either tubular or bivalve. A kind of Kelly cystoscope or endoscope of a diameter of 13.0, 14.5, and 16.0 mm. and a length of 40, 46, and 60 mm., respectively, is used by Hartman. Illumination is by a light passed in on a stalk, rather than one fast to the inside of the tube. A head mirror may be used instead. The handicap connected with the tubular forms is lack of ability to distend the upper fornices, where the vagina broadens. In order to provide an inexpensive bivalve I had the double blade used by Harvey Cushing in the nose cut off at 40 cm. on the posterior blade and 35 cm. on the anterior. A lateral handle would be better to guard against soiling by fecal extrusion. Preliminary emptying of the bowel by a finger in the vagina might prevent the nuisance of defecation during inspection, while emptiness of rectum will facilitate spread of the blades of the speculum.

In conclusion, we repeat that the rhesus monkey presents in its cervix so many aspects corresponding to like findings in women in the way of development, injury and inflammation, that it should constitute a valuable experimental animal, particularly if it can be infected with the gonococcus. The rugose cervix seen in a certain proportion of this and other simians is a rather rare find in women.

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DISCUSSION

DR. J. C. LITZENBERG, MINNEAPOLIS, MINN.—When I reported a young ovum between twenty and twenty-four days of age, we had to go to monkey embryology because human material available was inadequate for the necessary comparisons of embryos of different ages. We did find in the monkey, through conference with

Dr. Hartmann, an analogue to our human ovary. The work of Hartmann in endocrinology and ovulation and various other phases and studies in the monkeys, and their similarities to the human being, is familiar to all of you. But they have not been simply scientific studies; they have been attempts to take leaves from the discoveries in the monkey for application in women.

Dickinson's paper does the same thing, for what he has given us today is not simply comparative anatomy. He has made one suggestion, for example, that if this monkey can be infected with gonorrhea, we may learn some things that we do not know about gonorrhea in women. His calling attention to the fact that in the monkey we may do experimental work that we cannot do in women is thus of importance.

Animal experimentation is necessary in order to find out certain biologic and clinical facts, but we have always had to meet the objection that the findings in the white rat, in the mouse, and in the rabbit, may not be the same as in women. With this additional evidence which Dickinson has brought out we may have an animal which is so much nearer to the reactions of woman than any other animal, we may study problems hitherto impossible.

DR. RAYMOND SQUIER, NEW YORK, N. Y.—It is interesting to me that the monkey, which so closely parallels woman anatomically and physiologically, differs so much from her in certain biologic respects. There is some subtle chemical difference that makes the monkey practically refractive to such an organism as the gonococcus, which is infectious for woman. Therefore the monkey cannot be used in the study of gonococcal infections. Of course, this may well be a blessing, for otherwise great damage might be done to experimental colonies.

How deplorable it is also that women do not show the same ease of cervical dilatation during labor as monkeys do, in which animals, so far as I know, the clinical entity of cervical dystocia has not been encountered.

DR. FRED J. TAUSSIG, ST. LOUIS, MO.—There is opportunity for a great deal of valuable scientific work in the field of comparative pathology. Much work has been done on comparative anatomy but very little thus far on comparative pathology. Through it we might very well gain information on such subjects as the blighted ovum, the origin of the amniotic fluid, or the cause of the onset of labor.

DR. OTTO H. SCHWARZ, ST. LOUIS, MO.—I should like to ask Dickinson whether he has any information concerning the presence of myomas in the rhesus monkey. I have asked several veterinarians about this and they seem to have no information at all in regard to it.

DR. EDWARD A. SCHUMANN, PHILADELPHIA, PA.—If Dr. Schwarz will consult a very valuable work, which has small circulation but which is most interesting, he will find an answer to his question. It is called *Diseases in Wild Animals*, by Herbert Fox, a pathologist at the Zoological Gardens in Philadelphia. Myomas have been found and examined in the orang-utan and the rhesus monkey. There has been very little work done in comparative pathology, but this volume has a mine of information which is worth the reading of every student of pathology.

OBSERVATIONS UPON OVULATION IN PRIMATES*

ARTHUR H. MORSE, M.D., AND G. VAN WAGENEN, PH.D.,
NEW HAVEN, CONN.

(From the Department of Obstetrics and Gynecology Yale School of Medicine)

STATEMENTS with respect to an equal or an alternating ovulatory activity, a subject in which my associate, Dr. G. van Wagenen, and I have recently been interested, appear infrequently in gynecologic literature. Indeed we have met but two references with respect to this problem in women. The first occurs in the article by Fraenkel upon the physiology of the sex organs which is included in the *Handbook* of Halban and Seitz. This author indicates that in general the ovaries in women function alternately, not however in regular turns, but depending upon conditions which are as yet not understood.

The second and much more informative reference is that of Dickinson who, by repeated pelvic examinations, determined that both ovaries swell and become tender to pressure at the midmonth. These changes, however, do not affect both organs equally and in six instances, one ovary was found to be twice the size of the other. In another case in which alternation in activity occurred, the left ovary was enlarged at the time of two expected menstruations and the right once. Twice there was absence of palpable ovarian enlargement or tenderness, and possible absence of ovulation.

Although the observations just mentioned are limited, definite information is available with respect to an alternation of ovulatory function in certain of the lower animals.

Thus Edgar Allen observed that of 21 mice in which data were available for the number of ova produced at 2, 3, and sometimes 4 estrous periods, 4 showed marked and 2 slight alternation of function, while in the others the function was quite evenly divided. Mandl in his series of experiments upon rabbits encountered rarely, instances in which unilateral ovulation occurred. Fraenkel found 11 similar instances in an examination of 272 rabbits. Corner counted 131 fresh corpora lutea in the left and 89 in the right ovaries of 26 sows. The extremes were: left 10, right 0, left 3, right 0, left 2, right 6. Küpfer found that in cows both ovaries function regularly, but that the succession of ovulation is neither routine nor reciprocal. The ovulatory function in this species differs with each animal; sometimes one, sometimes the other ovary functions, although in general the right tends to be more active than the left.

With respect to primates, the largest number of observations upon the alternation of ovulation with which we are familiar are those of Hartman upon monkeys.

*Read at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25 to 27, 1936.

This author who conducted his investigation by rectal palpation or by laparotomy found that the ovulatory function does not necessarily alternate with regularity between the ovaries, but may involve the same ovary two or three times in succession. Table I taken from Hartman's paper details the findings in his animals. Of a total of 54 ovulations, 27 occurred from the right and 27 from the left ovary.

TABLE I. HARTMAN'S OBSERVATIONS, SUCCESSION OF OVULATORY FUNCTION

(r = right ovary; l = left ovary; - = no observation)

NO. OF ANIMAL	SUCCESSION	HOW DETERMINED
2	l, l, r, r, r, l, r, l	palp.
4	l, r, -, r, l	lap.
7	l, r	palp.
12	r, l	palp.
17	l (?), r (?), l, r	lap.
28	r, r, -, l, r, l, r	lap.
34	l, r	palp.
39	r, l	lap.
39	r, l, r, l	palp.
40	r, r, l, l	lap.
41	r, l, l	palp. and lap.
43	r, r	lap.
45	l, l, r, r, r, l	sections
63	r, l, r, l	lap.
64	r, l, r, l, l	palp.
69	l, r	lap.
79	r, r	lap.
79	l, r, l	lap. and palp.
99	l, r, l	palp.

Since this observation of Hartman is, as far as we know, the only one in which a series of cycles was followed in primates, it occurred to us that an additional report on this point as a part of our investigative project carried out upon the *Macacus rhesus* monkey might prove of interest. In our investigations of the ovulatory activity, we chose the direct method of observation by repeated laparotomies because we had other points in mind which could be determined only by direct visual examination of the ovary in situ. The present paper is concerned primarily with the ovarian findings in the animals in question.

In the present study 8 animals were employed, 6 of which were observed over a period of from thirteen to seventeen cycles. In 2 animals the observations were limited to 4 cycles in the first and to 7 cycles in the second. Including all 8 animals, a total of 94 cycles was studied. As a preliminary measure in order to determine that preoperative menstruation was normal, the animals were observed over a period of three months before the investigation was begun. They were then subjected to laparotomy between the thirteenth and sixteenth days, and the site of ovulation was determined by the presence of a fresh corpus luteum in the individual ovary. Nembutal proved a satisfactory anesthetic and strict surgical technic was employed. This and the care exercised by Dr. van Wagenen, who did the major number of the laparotomies, resulted in the formation of remarkably few postoperative adhesions. Except-

ing the skin suture of fine black silk, the abdominal wound was approximated with sutures of fine catgut. As can be seen from Table II the slight operative procedure which we employed had no effect upon the occurrence of the subsequent menstrual cycles.

In all, 94 laparotomies were performed during the corresponding cycles, and the presence or absence of a fresh corpus luteum determined. Eighty-six of these cycles were associated with ovulation, while in 8, menstruation was nonovulatory in character. Of the total number of menstrual cycles associated with the presence of a corpus luteum, the structure was present 52 times in the right and 34 times in the left ovary. The character of sequence or of alternation of ovulation in the individual animals is shown in Table II.

TABLE II. SUCCESSION OF OVULATORY FUNCTION

r = right ovary 0 = no ovulation
l = left ovary - = no observation

NO. OF ANIMAL	SUCCESSION	SUMMATION
M.m. 160	l, l, r, l, r, l, l, r, r, 0, -, r, 0, r, r	7 right, 5 left ovary 2 nonovulatory cycles
M.m. 188	r, l, r, r, r, r, -, r, 0, l, r, l, l, r, r	9 right, 4 left ovary 1 nonovulatory cycle
M.m. 189	l, r, r, 0, sick	
M.m. 191	r, r, l, -, r, r, l, l, -, r, l, l, r, l, r, r, l	8 right, 7 left ovary 0 nonovulatory cycles
M.m. 192	r, l, r, r, l, r, l, -, l, r, l, l, r, r, l, l, r, r	9 right, 8 left ovary 0 nonovulatory cycles
M.m. 193	l, r, r, l, -, -, r, l, r, r, l, l, r, l, l, 0	6 right, 7 left ovary 1 nonovulatory cycle
M.m. 195	r, l, r, l, 0, 0, -, -, r, r, r, 0, 0, r, r	7 right, 2 left ovary 4 nonovulatory cycles
M.m. 196	r, r, r, l, r, r, r, sick	6 right, 1 left ovary 0 nonovulatory cycles

The results of these observations are similar to those of Hartman quoted above, and in the first place confirm his observations that in the *Macacus rhesus* although the ovaries, as in other animals, must be subjected to the same hormonal influences, there is no rule for the sequence or for the alternation of ovulatory function. Indeed as was shown in one animal, Monkey 196, in which of a total of 7 observations the corpus luteum was found upon the right side in six, ovulatory activity may be confined to one ovary although the other organ is present and, as far as can be determined anatomically normal.

In this connection the findings of G. van Wagenen with respect to the incidence of ovulation in the monkey from which one ovary had been excised is of interest. In three of Dr. van Wagenen's unilaterally gonadectomized macaques, exploratory laparotomies showed that ovulation had taken place in 14 out of 20 cycles. The ovary was examined from the seventeenth to the twentieth day of the cycle and the presence of a newly ruptured follicle or a corpus luteum of good size and healthy ap-

pearance was taken as evidence of ovulation. The remains of the previous corpus luteum could always be seen in the expected position in the ovary.

Eight consecutive cycles were studied in two monkeys and four in the third. The first six observations were positive in one animal; the first four and the first three in the other two animals. In two animals bleeding from the uterus began on the third day following a laparotomy, giving short cycles of nineteen and twenty-one days. Ovulation did not occur in cycles initiated by these early bleedings. One ovulation was recorded without any observed menstruation.

In the second place the observation first emphasized by Corner in his study of ovulation and menstruation in *Macacus rhesus* and subsequently pointed out by others, that menstruation in the monkey may occur in the absence of ovulation, is again confirmed by our own work. With respect to this point Edgar Allen states that even in primates the hormone of the corpus luteum is not necessary for menstruation, for the follicles need not develop to the point of ovulation, and in monkeys usually do not during the spring and summer of the year. Successive periods of menstruation may occur during these nonovulating seasons and these menstrual periods are, as we have also noted, indistinguishable externally at least from those which occur during the mating season when ovulation is the rule. In addition, Allen has noted that in menstrual cycles without ovulation, the endometrium and mammary glands do not undergo the full premenstrual transformation, although the typical changes of edema in the subepithelial connective tissue and the extravasation of blood which immediately precedes the menstrual hemorrhage is present.

Novak has emphasized the possibility of human menstruation without ovulation, the periodic bleeding being indistinguishable from normal menstruation though at times there is some irregularity and some excess above the usual loss of blood. In his opinion a study of the endometrium will show, if ovulation has occurred, the characteristic secretory changes dependent upon the presence of the corpus luteum hormone. If, on the other hand, there is a complete absence of secretory changes, it may be assumed that ovulation has not occurred. The similarity of the histologic picture in the endometrium from such patients, to that found in monkeys in which it is known that menstrual bleeding has taken place in the absence of ovulation, would seem to support Novak's contention. Moreover, if, as Edgar Allen suggests, an insufficiency of the anterior pituitary gonad stimulating hormone may explain the frequent anovulatory menstrual cycle of monkeys a similar insufficiency may account for similar cycles in the human being.

Finally, in connection with the general question of the time and occurrence of ovulation a recent study made by Burr, Hill, and Allen is

pertinent. Burr and his associates have developed a vacuum tube potentiometer which is stable, draws almost no current from the living system and is independent of interelectrode resistance up to one megohm. With this instrument it is possible to record accurately minute voltage changes in living systems under a wide variety of circumstances.

Applying the apparatus to a study of ovulation in rabbits, it was found that readings taken previous to the eighth hour after mating, established a fairly uniform base line. Subsequently a distinct but gradual rise from the base line occurred. In the first rabbit as the ninth hour after mating approached, a sharp rise of potential occurred which was 45 times greater than the control variation. Twelve minutes later a similar change in potential was repeated. A third rise and fall occurred seventeen minutes after the second surge. Following these records an examination of the ovaries at laparotomy showed 3 rupture points, 2 in one ovary and 1 in the other. A comparison of the recordings obtained from other animals with their ovaries at laparotomy showed that in each animal the number of rises in potential equalled the number of ruptured follicles. As the authors indicate, these findings suggest that with the aid of this new instrument, it is possible to determine with great certainty in the intact animal the time and duration of ovulation, the instant of follicular rupture and the exact number of ovulations. While a study of ovulation in the human being has as yet not been carried out with this instrument, the results obtained suggest that similar results may be found in woman. If this proves to be the case there will be at hand an additional means for study, which should yield further information respecting the alternation of ovulatory function and anovulatory menstruation in woman.

To recapitulate, the present paper details the results of a study by repeated laparotomy of the alternation of ovulation in the *Macacus rhesus* monkey. In addition, it speaks briefly of the problem of anovulatory menstruation and of the recent method for the detection of ovulation devised by Burr, Hill and Allen.

We wish to acknowledge our indebtedness for assistance to our laboratory technicians, Miss Ruth Vogel and Mr. Joseph Negri. The study was subsidized by a grant from the Research Fund of the School of Medicine.

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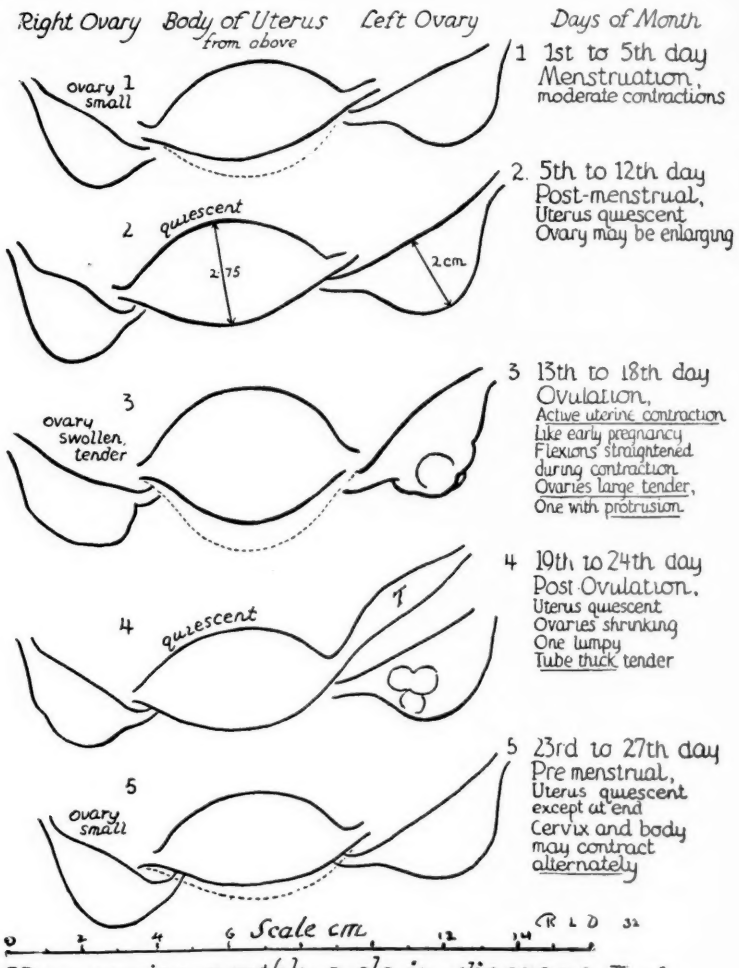
DISCUSSION

DR. ROBERT L. DICKINSON, New York, N. Y.—The time of ovulation may be profitably studied in women by bimanual palpation, but from my experience with both, it is vastly more difficult than in small monkeys. With patients with relaxed abdominal wall, one or both ovaries may be caught and outlined, the right against



Utero-ovarian monthly cycle in diagrams Fig 1

the lateral pelvic wall, the left between the fingertips of the outer and inner hand. Thus the enlarged follicle or the corpus luteum can be detected. An easier procedure is the seizure of the body of the uterus and the recognition of definite contraction and relaxation in its rhythmic activity, which is pronounced during the days of maximum distention of the follicle in many women.

Any procedure which would date ovulation in a given individual would help in the selection of times for desired conception, and safety from conception. Examina-

tions would only be needed to find the time of active contractions, and they are superfluous when ovulation is indicated by pelvic ache, by ovarian tenderness, or self-palpation or by breast ache. Five patients were examined at two- or three-day intervals for three months, at the same time of day, with empty bowel, and yielded

89 observations. In addition, some records of Mittelschmerz were examined, and my early publications were drawn upon. These data point to the following conclusions:

1. The uterus in the nonpregnant exhibits steadily recurring rhythmic contractions and relaxations.

2. The intervals range from two to twenty minutes, as found by palpation.

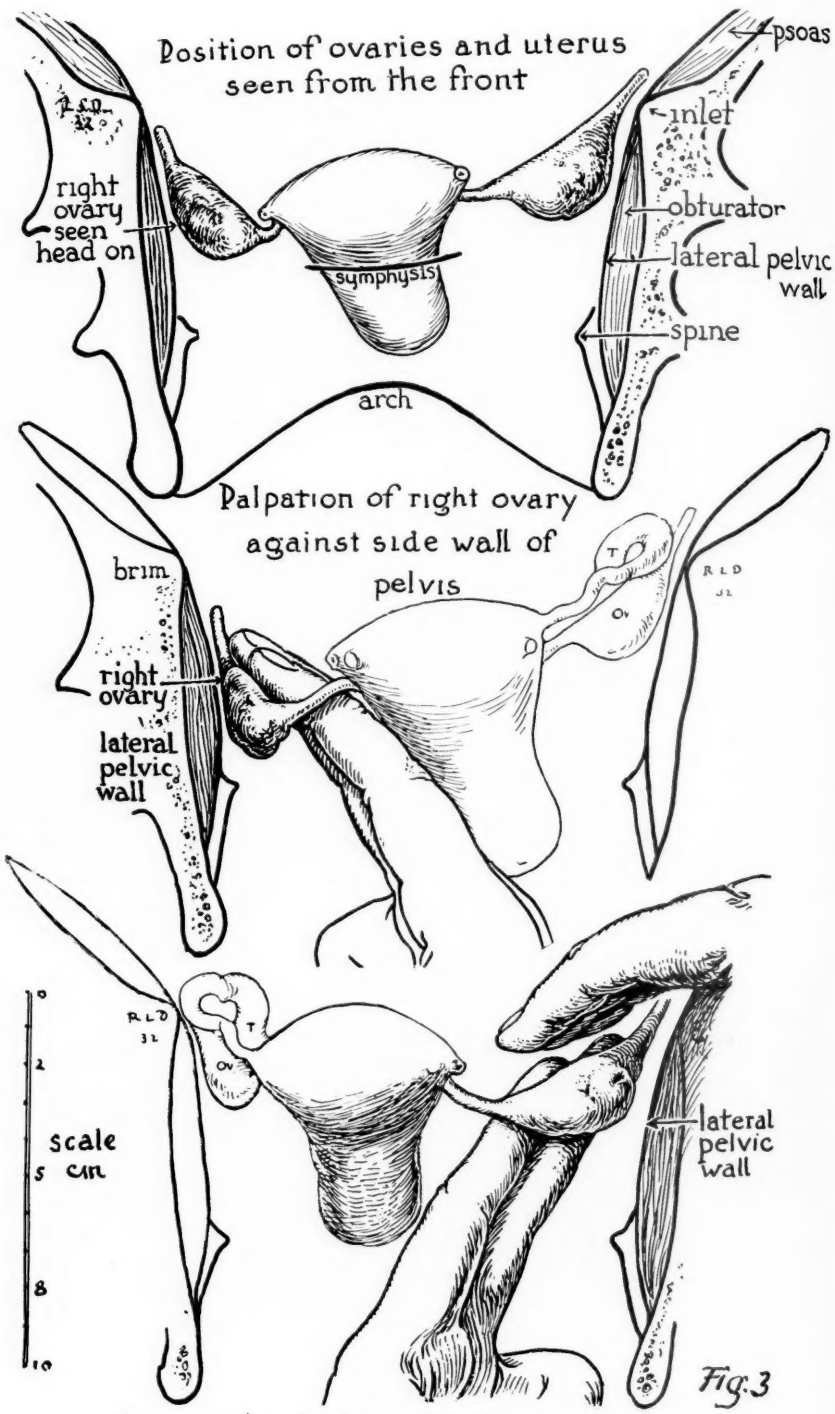


Fig. 3

Bimanual palpation of left ovary with uterus pushed to right

3. These contractions fall into three main periods, one of major activity at or about the time of ovarian enlargement, preceded and followed by periods of relative quiescence.

4. Before and during menstruation a minor increase in frequency and excitability may be found.

5. In examining the uterus during ovulation, the findings suggest early pregnancy as do also the vacillations in the size and compressibility of various segments found while palpating.

6. Both ovaries enlarge and become tender, and one may have a protruding mass, while later the corresponding tube may swell.

7. During contraction any flexion (normal or otherwise) partially straightens out.

8. Corpus and cervix may alternate in rhythm.

9. A wave of contraction may be found starting in the cervix, passing to the isthmus, and thence to the corpus. Except in isolated isthmus relaxation (Hegar's sign) the isthmus usually acts with the corpus.

Both ovaries swell and become tender to pressure at the midmonth, but one more so than the other, in six instances one being recorded as "twice the size of the opposite ovary." On the larger ovary a protruding mass may be found. A couple of days later, with lessened size and tension, a nodular feel like a "blackberry" has been noted.

One ovary may do more than its share, the left seeming to be the more active, both in palpated patients and from my "Mittelschmerz" reports. With midperiod pain both sides usually ache or are tender to the patient's pressure on the lower abdomen, but when asked to record the relative degree of tenderness or pain between one ovary and its fellow, several patients report alternation between one month and the next. In one case personally studied three months' alternation in activity occurred, the left ovary being enlarged twice at the expected time, and the right once, but three days late. Twice there was absence of palpable ovarian enlargement or tenderness at the midmonth, suggesting a possible absence of ovulation.

Tubal thickening and tenderness have been observed a few days after the supposed date of ovulation, on the side of the affected ovary, in four instances.

The patient seemed to adhere to a given time in the cycle within three days, in the five palpated and in six midpain patients. In one case the findings of three periods pointed to the thirteenth, fourteenth, and seventeenth day, respectively. Yet one palpated patient showed uterine changes on the ninth day once, on the sixteenth day once, and the findings were uncertain once.

DR. RAYMOND SQUIER, NEW YORK, N. Y. (by invitation).—It seems to me that one interesting direction that research in ovulation will take is toward the quality of the ovum. Whereas the factors responsible for the mechanical release of the egg from the ovary are coming to be increasingly well known, what develops the ovum itself remains a mystery.

The quality of ova, as Streeter and associates have emphasized, has an important bearing on spontaneous abortion. We know that among laboratory animals as many as one-fifth of ova are sufficiently defective to be so recognized microscopically, as early as the time of ovulation. Further abnormalities show up later, perhaps either preventing implantation or causing subsequent abortion of the conceptus at any stage of gestation.

The existence of nonovulatory menstrual cycles in the monkey, especially during the summer in this latitude, has been well established by Hartman and Corner, and there is accumulating clinical evidence that they occur in women.

These two lines of interest may some day converge for the answer to this interesting question: Just as there are variations, seasonal or other, in the incidence of ovulation, may there not be also variations, parallel or independent thereof, in the incidence of defective ova? Such variation might be reflected as temporary sterility or as spontaneous abortion.

THE SIZE AND SHAPE OF THE PELVIC INLET AS DETERMINED BY DIRECT MEASUREMENT*

EDWARD A. SCHUMANN, A.B., M.D., F.A.C.S., PHILADELPHIA, PA.

THE work of Caldwell and Moloy, Thoms, Jarcho and others has again drawn the attention of obstetricians to the architecture of the pelvis. In view of the various opinions expressed as to the size and shape of the pelvic inlet, it was determined to measure a series of pelves directly through the abdominal incision, in patients subjected to laparotomy, for various gynecologic lesions. Accordingly, a number of pelves were so measured at the Kensington Hospital for Women, the technic being to determine the length of the anteroposterior and greatest transverse diameter of the inlet, with a De Lee outlet pelvimeter. This was easily accomplished by inserting the instrument through the abdominal incision and then, while the operator controlled the position of the tips to insure their being correctly placed, the assistant spread the handles of the pelvimeter and read the scale. These measurements were carried out during the course of abdominal operations and the patients were not selected, but taken consecutively. During the period of convalescence, careful external pelvimetry was performed on all these women, and their obstetric histories, if any, were obtained, the results being correlated as shown in Tables I to IV.

As a result of this investigation, certain definite conclusions were drawn. First, that the oval inlet is more common than any other type, 40 per cent of our cases possessing such oval pelves of ample size, while another 26 per cent presented oval pelves of the flat type. Next in order were the round pelvic inlets, which accounted for 24 per cent, and still less frequent was the anthropoid type, which was found in 10 per cent of the cases studied.

A considerable series of patients was investigated but, inasmuch as there was no variation in the occurrence of the different types, only the first fifty cases are here analyzed in detail.

In the oval pelves of large size the anteroposterior diameter varied from 10.5 cm. to 12.25 cm., the average being 11 cm. The transverse varied from 12 cm. to 13 cm., the average being 12.25 cm. It is interest-

*Read at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25 to 27, 1936.

ing to note that the largest pelvis measured belonged to this group, its diameter being 12.25 by 14 cm., the patient having a double uterus but having never been pregnant. Of the small and flat oval pelves, the anteroposterior diameter varied from 9.5 to 10.5 cm., the average being

TABLE I. OVAL PELVES, LARGE

CASE	MEASUREMENT OF INLET		EXTERNAL PELVIMETRY				OBSTETRIC HISTORY	
	A. P.	TR.	I. S.	I. C.	TROCH.	EX. CON.	NUMBER OF CHILDREN	WEIGHT POUNDS
2	10.5	× 12.5	24.5	28.0	29.0	19.0	1	7
4	11.0	× 12.5	27.5	31.0	32.5	20.5	2	7¾-8½
9	10.75	× 12.0	27.0	29.0	34.0	20.0	1	8
10	11.25	× 12.5	25.0	27.5	32.0	22.0	1	7½
12	11.0	× 12.25	27.0	30.0	34.0	22.0	4	Full size
14	11.25	× 12.75	25.0	28.0	31.0	19.5	None	
15	10.75	× 12.0	24.0	26.0	29.5	18.0	None	
21	10.75	× 12.75	27.0	30.0	34.0	20.5	2	7-13
23	11.0	× 13.0	26.0	29.0	32.5	19.5	1	6¾
24	11.5	× 12.25	27.0	30.0	32.0	22.0	1	9½
27	11.75	× 12.5	25.0	28.0	31.0	20.0	None	
32	11.0	× 11.5	27.0	29.0	33.5	20.0	1	7
36	11.5	× 12.25	28.0	30.0	31.0	20.0	1	6
38	11.0	× 13.0	25.0	27.0	30.0	19.0	None	
40	11.25	× 12.25	25.0	29.0	32.0	20.0	3	7-6-8
43	12.25	× 14.0	31.0	32.0	37.0	20.0	None (double uterus)	
50	12.5	× 13.0	28.0	31.0	33.5	21.5	1	8
31	11.25	× 12.0	26.0	27.0	32.0	18.5	4	8½-8-7-7½
42	10.5	× 12.5	27.0	29.0	33.0	18.5	11	All spon.
44	10.5	× 11.0	25.0	27.0	31.0	20.0	None	

TABLE II. OVAL PELVES, SMALL; ALSO FLAT TYPE

CASE	MEASUREMENT OF INLET		EXTERNAL PELVIMETRY				OBSTETRIC HISTORY	
	A. P.	TR.	I. S.	I. C.	TROCH.	EX. CON.	NUMBER OF CHILDREN	WEIGHT POUNDS
5	10.0	× 11.0	22.0	25.0	28.0	18.5	2	6-6½
6	10.5	× 12.5	23.0	26.0	29.0	17.5	1 (forceps)	8
7	10.5	× 13.0	24.0	28.0	30.0	19.0	4	10-10-9¾
8	9.5	× 12.0	30.0	31.0	22.0	7.0	1 (forceps)	7
16	10.0	× 12.0	24.0	26.5	31.0	20.0	8	Unknown
19	10.0	× 12.25	26.5	29.75	30.25	19.0	None	
20	9.75	× 11.0	27.0	28.5	32.0	17.5	2 (both forceps)	4-4
25	10.25	× 13.5	27.0	30.0	32.0	22.0	4	6-7-7-8
28	9.5	× 11.0	26.5	27.5	32.0	20.0	3	8-7-4½
34	10.0	× 11.5	25.0	28.0	32.0	20.5	1	7
35	9.0	× 13.0	26.0	27.0	30.0	22.0	7 (1 forceps)	Children all large.
46	10.0	× 12.0	25.5	27.5	31.0	17.0	1	7
48	10.0	× 12.0	24.0	27.0	28.5	18.5	None	

10 cm., while the transverse on the average was 12. The round pelves averaged 11.5 by 11.5 cm. Another interesting point is that, although 38 of the 50 patients examined had borne one or more children, none of them had had any particular obstetric difficulties, and only six had required instrumental deliveries.

In no patient was any marked pelvic contraction observed. The external pelvimetry, which was carefully performed in all of these patients, is noteworthy by the fact that the figures so obtained bear little or no relation to the actual size of the pelvic inlet. This is true of all the external diameters but particularly impressive in the external conjugate, which varied within wide limits from the true conjugate.

It would seem that external pelvimetry must be more and more disregarded as a means of obstetric diagnosis, because the gross errors

TABLE III. ROUND INLETS

CASE	MEASUREMENT OF INLET		EXTERNAL PELVIMETRY				OBSTETRIC HISTORY	
	A. P.	TR.	I. S.	I. C.	TROCH.	EX. CON.	NUMBER OF CHILDREN	WEIGHT POUNDS
1	12.25 ×	12.25	26.5	29.5	33.0	20.5	None	
11	12.5 ×	12.5	29.0	33.0	35.0	21.0	3	8-8-9 spon.
17	11.0 ×	11.0	27.0	29.0	33.0	20.0	3	8-9-8¾ spon.
18	11.5 ×	11.5	24.5	27.1	30.0	19.5	None	
26	11.5 ×	11.5	25.0	29.0	30.0	21.0	1 (forceps long labor)	Weight not known
29	12.25 ×	12.5	27.0	30.0	33.0	21.0	3	8-6-9 spon.
41	11.5 ×	11.5	26.0	28.0	31.5	19.5	None	
45	11.25 ×	11.5	25.5	28.0	33.0	21.0	2	7-11
47	11.5 ×	11.5	26.5	29.0	33.5	21.0	2	7-4
49	11.5 ×	11.5	24.0	26.5	29.0	18.0	2	5-4
3	12.0 ×	12.5	25.5	27.5	31.0	19.0	None	
13	12.0 ×	12.5	25.0	29.0	33.0	21.0	None	

TABLE IV. ANTHROPOID PELVIS

CASE	MEASUREMENT OF INLET		EXTERNAL PELVIMETRY				OBSTETRIC HISTORY	
	A. P.	TR.	I. S.	I. C.	TROCH.	EX. CON.	NUMBER OF CHILDREN	WEIGHT POUNDS
22	13.0 ×	12.25	24.5	26.5	33.0	22.0	2	10-7
30	13.0 ×	11.5	25.0	28.0	31.5	20.5	2	6 premat.
33	12.5 ×	11.5	28.0	31.0	33.0	23.0	6	Average size
37	11.5 ×	11.0	22.5	26.0	30.0	18.0	None	
39	12.0 ×	11.5	27.0	29.0	33.0	21.0	3	6½-6-9

involved in it may well lead the inexperienced obstetrician into a false sense of security, when in point of fact, severe pelvic contraction may exist.

In order to determine the accuracy of roentgenologic measurement of the pelvis, a group of the foregoing patients were subjected to measurement by the technic of Thoms, and it was extremely gratifying to learn that the diameters of the inlet as determined by direct intra-abdominal measurement corresponded in every instance with those obtained by this technic, the variation being constantly less than 2 mm.

The conclusions reached from this investigation are:

1. That the oval pelvis is much the most frequent type met, followed in order by the round and the anthropoid forms.

2. That external pelvic measurements are unreliable as indicators of the true size of the inlet.

3. And last, that the technic of Thoms may be relied upon as an accurate method of evaluating pelvic size and shape.

1814 SPRUCE STREET

DISCUSSION

DR. ALFRED C. BECK, BROOKLYN, N. Y.—This method of direct measurement of the pelvic inlet is simple and apparently very accurate. It should be useful to those of us who do both obstetrics and gynecology. We now can easily measure the inlet of those women in the reproductive period who are subjected to laparotomy. Its use ought to be particularly indicated in the nulliparous woman and in those who have had trouble in a previous labor.

I was pleased to hear Dr. Schumann state that he also found that external pelvimetry is unreliable, but that this method, when used to check the work of Dr. Thoms, indicated that his x-ray observations were very accurate. I believe that Dr. Thoms' x-ray observations are among the significant contributions made to obstetrics in our time.

(American Gynecological Society papers to be concluded in the December issue.)

THE INVESTIGATION OF A NEW PENTAVALENT ARSENICAL, ALDARSONE, IN THE TREATMENT OF TRICHOMONAS VAGINITIS*

P. BROOKE BLAND, M.D., AND A. E. RAKOFF, A.B., PHILADELPHIA, PA.
(From the Department of Obstetrics, Jefferson Medical College Hospital)

A SURVEY of the recent literature indicates that the treatment of trichomonas vaginitis by drying plus antisepsis has largely replaced the use of liquid antiseptics.

The technic for the dry antiseptic treatment consists generally of a preliminary washing of the vagina and external genitalia by some mild liquid antiseptic or cleansing agent, drying, followed by the application of the active drug in the form of a powder, tablet, paste or ointment. Many chemotherapeutic agents have been thus employed as trichomonadicidal drugs, including Lassar's paste,[20] zinc oxide ointment,[21] kaolin,[3] cornstarch,[19] metaphen ointment,[6] quinine sulphate,[17] salicylic acid,[12] sodium bicarbonate,[2] and acetarsone.[13]

The excellent results of treatment of various protozoan diseases by organic arsenicals prompted the usage of acetarsone, in the form of tablets and powder mixtures for the dry treatment of vaginal trichomoniasis.

*The laboratory investigation of aldarsone was aided by a grant from the Abbott Laboratories, North Chicago, Ill.

Laboratory investigation of aldarsone (preparation No. 1,717), a soluble pentavalent organic arsenical chemically related to acetarsone, which has recently been synthesized and described by Raiziss, Severac and Kremens,[22] led to the discovery that this compound* has many times the trichomonadicidal power of acetarsone, is less toxic, and has the additional advantage of being highly hygroscopic.

In view of these laboratory findings an extensive series of clinical observations were also undertaken to evaluate the efficacy of aldarsone in the treatment of vaginal trichomoniasis. Similar studies with acetarsone were conducted simultaneously in order to afford an adequate basis of comparison.

MATERIALS AND METHODS

Experiments in vitro.—The trichomonadicidal power of aldarsone and acetarsone were determined by the following method.

Various concentrations of the drugs in distilled water were prepared. In the case of aldarsone, clear pale yellow solutions were obtained, while acetarsone yielded heavy white suspensions. Solutions of acetarsone were prepared by adding sufficient sodium bicarbonate to dissolve the arsenical.

One-half cubic centimeter of the preparation to be tested was mixed in a small test tube with an equal quantity of a heavy suspension of freshly collected vaginal material in Ringer's solution, containing numerous active trichomonads. The final concentration of the drug was therefore one-half that of the original preparation.

At the instant of contact of the drug with the organisms a stop watch was started. After a few seconds of vigorous mixing a drop of the mixture was placed on a glass slip and observed under the microscope, first with the low power lens and then more minutely with the high dry objective. The time was recorded when total cessation of movement had occurred in all the organisms. Since the flagella and undulating membrane may continue slow rhythmic motion for some time after actual displacement of the organism has ceased, these structures must be carefully focused upon.

If death of the organisms did not occur within a few minutes, observation was continued upon a fresh drop. Each observation was repeated three times and an average was taken.

To note the influence of additional organic material upon the trichomonadicidal power of the drug, experiments were also performed with solutions and suspensions of the drugs in human blood serum.

CLINICAL STUDIES

A total of 135 patients in attendance at the antenatal and postnatal clinics of the Department of Obstetrics, Jefferson Medical College Hospital, Philadelphia, were treated for trichomonas vaginitis. Ninety-six were pregnant women in the first, second, or early weeks of the third trimester of gestation, while 39 were nongravid patients. The patients selected exhibited clinical and microscopic evidence of infestation with *Trichomonas vaginalis.*

One hundred women were treated with aldarsone, 25 received treatment with acetarsone, while in 10 patients used as control subjects, kaolin alone was used.

*This drug was prepared and supplied for this study by the Dermatological Research Laboratories, Philadelphia, Division of Abbott Laboratories, North Chicago, Ill.

The following technic was employed in the treatment of these women:

With the patient in the lithotomy position, the vagina was exposed with a bivalve speculum and the mucosa thoroughly washed with a diluted tincture of green soap and water. The vaginal membrane was then thoroughly dried with cotton pledgets.

The vaginal portion of the cervix was painted with tincture of metaphen, and a number of applicators dipped in the solution were successively carried deep into the cervical canal.

The introitus and vulva were thoroughly scrubbed with tincture of green soap and water, and then dried.

The urethra and paraurethral recesses were treated with an aqueous solution of metaphen 1:500, repeatedly applied on cotton applicators.

The antiseptic powder preparation was insufflated into the vagina with a powder blower. One-half gram of the arsenical with finely divided kaolin sufficient to make 3 gm. was used for each treatment. A number of vaginal insufflators were successfully used, including the Gellhorn powder blower,[13] the Powdex insufflator, the Shelanski insufflator, and several designed by Dr. G. W. Raiziss.

The patient was treated in this manner on three consecutive days. Three additional treatments were given at three-day intervals. The patient was instructed not to douche and to refrain from intercourse during the period of treatment.

A microscopic research for trichomonads was made before each treatment and at regular intervals thereafter. Smears from the vagina and cervix were taken to note changes in the bacterial flora.

In a number of instances, because of failure of cooperation on the part of the patients, completion of the series of treatments or posttreatment check-ups was not possible. The records of such patients were withdrawn from the study and replaced by others.

RESULTS

Studies in vitro.—The killing time of solutions of aldarsone of a number of concentrations for *Trichomonas vaginalis* are given in Table I. The range among the ten strains of trichomonads tested, as well as the calculated average killing time is given.

TABLE I. RESULTS OF EXPOSURE OF TEN STRAINS OF TRICHOMONAS VAGINALIS TO ALDARSONE AND ACETARSONE (MICROSCOPIC EXAMINATION)

DRUG	FINAL CONCENTRATION OF DRUG IN TEST MIXTURE	RESULTS	
		AVERAGE KILLING TIME	RANGE
Aldarsone	1:10	At once*	--------
	1:20	20″	At once to 90″
	1:30	4′ 40″	4′ 15″ to 7′
	1:40	13′ 50″	6′ to 22′ 30″
Acetarsone	Saturated Solution	Actively motile after 1 hour	
	1:20 Suspension	Slowly motile or "rounded up" with flagella still beating, after 1 hour	
	1:20 Solution (Dissolved by addition of $NaHCO_3$)	Actively motile after 1 hour	

*Approximately fifteen seconds are required to make an initial observation.

In concentrations of aldarsone up to 1:10 all strains were killed at once, that is before they could be observed under the microscope. Aldarsone 1:20 had an average killing time of twenty seconds.

Table II reveals that large concentrations of organic material had little effect on the trichomonadicidal power of aldarsone. Solutions of aldarsone 1:30 in 25 per cent human blood serum and in distilled water were almost equally effective. It will be recalled that considerable quantities of organic material were present in all of the test mixtures, since one-half of the test preparation consisted of a heavy suspension of vaginal secretion in saline.

The results with acetarsone (Table I) indicate a comparatively low trichomonadicidal power.

The ten strains of organisms studied were all actively motile after an exposure of one hour to a saturated solution of acetarsone. In a suspension of acetarsone, in which its final concentration was 1:20, the organisms were either slowly motile or "rounded up" with flagella still beating after an exposure of one hour.

The trichomonadicidal power of a carbonated solution of acetarsone 1:20 was even lower than the suspension, since in every instance the organisms were actively motile after one hour.

TABLE II. EFFECT OF HUMAN BLOOD SERUM ON TRICHOMONADICIDAL POWER OF ALDARSONE

SOLUTION TESTED	FINAL CONCENTRATION OF ALDARSONE IN TEST MIXTURE	AVERAGE KILLING TIME (5 TESTS)
Aldarsone 1:15 in 50 per cent human blood serum	1:30*	5′ 35″
Aldarsone 1:15 in distilled water	1:30	5′ 20″

*In the final test mixture the concentration of human blood serum is 25 per cent.

Clinical Results.—The results of treatment of 135 patients with trichomonas vaginitis are given in Tables III and IV, based on the findings at the last periodic examination, three to nine months after treatment.

It is shown in Table III that 84 per cent of 100 patients responded to a series of 6 treatments of aldarsone and have since remained microscopically negative. Of the 16 patients who had recurrences, 5 remained negative following 6 additional treatments, and 3 required a total of 18 treatments.

TABLE III. RESULTS OF TREATMENT

	ALDARSONE	ACETARSONE
Total No. of patients treated	100	25
Total No. remaining free from trichomonas	91 or 91%	12 or 44.4%
Required 6 treatments	84 or 84%	7 or 28.0%
Required 12 treatments	5 or 5%	2 or 8%
Required 18 treatments	2 or 2%	2 or 8%
Total No. not cured	9 or 9%	13 or 55.6%

TABLE IV. PERIOD OF OBSERVATION OF PATIENTS TREATED WITH ALDARSONE AND THEIR PRESENT STATUS

PERIOD OF OBSERVATION	NO. OF PATIENTS	PRESENT STATUS	
		NEGATIVE	POSITIVE
9 months	5	5	0
8 months	10	10	0
7 months	19	16	3
6 months	25	22	3
5 months	14	13	1
4 months	16	15	1
3 months	11	10	1
	100	91	9

In 3 nonpregnant women badly eroded cervices were treated with the electric cautery before the institution of the third series of treatments, with the result that in 2 of these women cures were obtained.

Of the total group of 100, nine are still clinically and microscopically positive.

Permanent disappearance of the trichomonads was invariably accompanied by a disappearance of the leucorrhea. Generally the microscopic appearance of the secretion returned to normal, together with the appearance of the normal bacterial flora. In a few instances the profuse leucorrhea of vaginal trichomoniasis was replaced by a moderate white mucopurulent discharge, resulting from cervical disease.

In Table IV a résumé of the period of time is given during which the patients have been observed together with a tabulation of their present status. It will be noted that 59 patients have been observed for six to nine months, while the remaining 41 have been followed for three to six months.

A comparison of the results obtained among pregnant and nonpregnant patients treated with aldarsone is presented in Table V. The end-results for each group are approximately equal, 91.7 per cent of 72 pregnant patients remained negative, compared to 89.3 per cent of 28 nonpregnant women.

Recurrences were tabulated after each series of six treatments. Sixteen recurrences were noted following the first series of treatments with aldarsone among 100 patients. A second recurrence was obtained in 11 of the 16 patients, after a second series of treatments. Nine women had a third recurrence following the third group of treatments.

The total of 36 recurrences have been classified in Table VI, with reference to the interval of time which elapsed between the last treatment and the time when the recurrence was noted. More than half of these occurred in the first two weeks of observation, while the remainder were noted at intervals up to eight weeks. No relapses occurred after a period of negativity of eight weeks in patients observed for three to nine months.

TABLE V. COMPARISON OF RESULTS OF TREATMENT WITH ALDARSONE AMONG PREGNANT AND NONPREGNANT PATIENTS

	PREGNANT PATIENTS	NONPREGNANT PATIENTS
Total number treated	72	28
Total number remaining negative	66 or 91.7%	25 or 89.3%
Required 6 treatments	61 or 84.7%	23 or 82.2%
Required 12 treatments	5 or 6.9%	0
Required 18 treatments	0	2 or 7.1%
Total number not cured	6 or 8.3%	3 or 10.7%

TABLE VI. ANALYSIS OF RECURRENCES FOLLOWING TREATMENT WITH ALDARSONE

Following first 6 treatments	16
Following second series of 6 treatments	11
Following third series of 6 treatments	9
	36
During first two weeks	22
Second to fourth week	7
Fourth to sixth week	4
Sixth to eighth week	3
Eighth to thirty-sixth week	0
	36

Of 23 recurrences among pregnant women, only 2 were noted after delivery.

Among the nonpregnant women the recurrences were noted chiefly after the next menstrual period, and occasionally not until the second menstrual period following the treatment.

The results of treatment with acetarsone are given in Table III.

Eleven or 44.4 per cent of 25 patients treated remained negative after a period of observation of six to eight months. Seven of the patients cured remained negative after six treatments, 2 patients required an additional series of treatments, while 2 others remained negative after 2 additional series of treatments. Thirteen or 55.6 per cent of the group remained uncured after a total of 18 treatments with acetarsone.

Seventeen of the women in this group were pregnant, while 8 were nongravidas. The percentage of cures in the pregnant group (50 per cent) was somewhat greater than in the nonpregnant group (41.2 per cent).

Of the 10 control patients one has remained free from *T. vaginalis* after a period of six months, following 6 treatments in which kaolin alone was used for insufflation, after preliminary treatment with tincture of green soap, and the application of metaphen to the cervix and urethra. The other 9 controls received 3 series of 6 treatments, following which recurrences were noted in each instance.

In no instance were toxic symptoms or other reactions following the administration of acetarsone or aldarsone noted, although as many as 18 treatments using a total of 9 gm. of the arsenicals were administered to a number of patients during the course of five weeks.

DISCUSSION

Although many antiseptics have a high trichomonadicidal power in vitro, relatively few are clinically effective. The inability of these drugs to keep the vagina proper free from organisms may be the result of their rapid absorption, their inactivation within the vagina, or the fact that they are diluted and drained away from the vaginal canal.

The good results following the insufflation of antiseptic powders is in large measure the result of the long-continued action of the drug, thus not only destroying organisms with which they come into contact, but also inhibiting reinfestation by those that are not reached. In addition the maintenance of a dry vagina which is favored by powders, is in itself inimical to multiplication of trichomonads. It is well known that as soon as a drop of secretion has been dried all of the flagellates within it are destroyed. The advantages of treatment by drying plus antisepsis have been especially emphasized by Kleegman.[20]

In this connection attention is drawn to the fact that 1 of 10 control patients was cured merely by repeated mechanical cleansing and drying followed by insufflation of kaolin, while in several other instances recurrences were not noted until one or two weeks after treatment.

Acetarsone has been used in trichomonas vaginitis as the active ingredient of tablets introduced under the trade name of devegan. According to Fuge,[11] each tablet contains 0.25 gm. of acetarsone, 0.03 gm. of boric acid, and 0.67 gm. of carbohydrate.

Although a number of the German writers have referred to devegan as a "specific," few statistics of the results of treatment are available.

Fuge[11] inserts 1 or 2 devegan tablets within the vagina daily for ten days. Of 100 patients treated, 60 were reported free from recurrence, while the others were still under observation. The criteria of a cure or the period through which the patients were watched for recurrences are not stated.

Hees[16] claimed 95 per cent cures in over 100 cases and stated that the others responded to continued treatment.

Ackermann[1] observed 25 patients following treatment with devegan. Twelve were negative after a period of observation ranging from two to thirty-three weeks, while in 13 patients recurrences were noted.

Hajek[15] and Rodecurt[23] also advocate the use of devegan.

In this country the use of devegan has been reported by Karnaky,[18] who noted that 200 patients treated with this preparation were relieved of symptoms so long as they continued the use of devegan. Karnaky, however, fails to state how many of this group were permanently cured.

A mixture containing 12.5 per cent of acetarsone in equal parts of kaolin and sodium bicarbonate was recommended by Gellhorn.[13] One teaspoonful of the mixture was insufflated by means of a powder blower designed to distribute the compound over the vaginal mucosa. The superiority of this method of introducing the arsenical lies in the fact that organisms throughout the vagina are reached, whereas the insertion of tablets leaves many parts of the vaginal mucosa untreated.

The drying effect of kaolin recommends this substance as a diluent. The value of the sodium bicarbonate is, however, questionable. The alkaline reaction of this substance tends to dissolve acetarsone. Our studies in vitro indicate, however, that solutions of acetarsone have even less trichomonadicidal activity than suspensions of acetarsone of equal percentage.

The use of boric acid and glycolyzed carbohydrates as employed in devegan on the basis that the acid medium and additional carbohydrate will favor the return of Döderlein's bacilli, also appears to be superfluous. It is well known that in trichomonas vaginitis the secretion is already markedly acid, Cruickshank and Sharman[8] noting that the pH varied from 4.9 to 6.0, while Fukishima[12] found considerable concentrations of lactic acid. In cases of vaginal trichomoniasis uncomplicated by cervical infections, we have repeatedly noted the appearance of large numbers of Döderlein's bacilli, as the trichomonads disappeared after treatment by various methods. Indeed it is our opinion[5] that the permanent reestablishment of the normal bacterial flora is the most reliable indication of a permanent cure.

Gellhorn's method of treatment has also been endorsed by J. C. Smith.[24] Neither of these investigators, however, have reported statistical results of their treatment.

Goldstein[14] recommends the addition of 1.5 gr. of salicylic acid to Gellhorn's formula. Crossen and Crossen[7] also believe this mixture to be efficacious.

Aldarsone.—The synthesis of the pentavalent arsenical, aldarsone (sodium-methylene-sulphon-amino-hydroxy-phenyl-arsonate), was re-

cently described by Raiziss, Severac and Kremens[22] as preparation No. 1,717. Chemically it is a condensation product of 3-amino-4-hydroxy-phenylarsonic acid with sodium formaldehyde sulphoxylate.

Aldarsone is a white amorphous powder, very soluble in water, but insoluble in alcohol, ether, acetone, or chloroform. The aqueous solution is neutral or slightly alkaline having a pH about 7.6. The product contains about 18 per cent of arsenic and 7 per cent of sulphur. In a therapeutic study of the new product in the treatment of syphilitic rabbits, Raiziss and his associates[22] noted a definite spirocheticidal power which was superior to that of tryparsamide, and compared favorably with acetarsone. When given intravenously to rats and rabbits the toxicity of the drug was lower than that of acetarsone, while on oral administration to rabbits its toxicity was of the same order of magnitude as that of acetarsone.

Our studies in vitro show that aldarsone is far superior to acetarsone as a trichomonadicide.

Davis[10] noted that a saturated solution of acetarsone did not kill *Trichomonas vaginalis* after fifteen minutes. In the present study, it was found that the organisms were still actively motile after being exposed to a saturated solution for one hour.

The hygroscopic quality and the lower toxicity of aldarsone were also considered to be definite advantages over acetarsone.

The free solubility of aldarsone assures its diffusion throughout the vagina, and indicates some degree of penetration. On the other hand, the insoluble acetarsone probably remains within the vagina for a longer period of time. Practically it was found that preliminary drying of the vagina plus the use of kaolin as a base insured the presence of considerable quantities of either drug within the vagina for a period of twelve to thirty-six hours.

The clinical study of aldarsone in the treatment of trichomonas vaginitis has confirmed the therapeutic efficiency which was anticipated as a result of the laboratory investigation. When administered by a thorough method of application, the clinical results were far superior to those resulting from the use of acetarsone.

Eighty-four of the 93 patients who were cured responded to an initial series of 6 treatments, 3 of which were given on consecutive days, while 3 others were given at three-day intervals. Preliminary studies have indicated that the 3 treatments which are given at daily intervals are essential for good results. We have found it to be a general principle in the treatment of trichomonas vaginitis that a number of treatments given at daily intervals are much more effective than a large series of treatments given at longer intervals.

Results of Treatment in Pregnancy.—A number of the methods described for the treatment of trichomonas vaginitis are obviously too

rigorous for application to pregnant women. As a result palliative measures, such as frequent douching, have been frequently recommended to tide the patient over until some time after delivery.

The method of treatment described in the present study, has proved to be as applicable to the obstetric as to the gynecologic patient.

Approximately three-fourths of the patients treated in the present study were pregnant women. In both the patients treated with aldarsone and with acetarsone, the percentage of cures was slightly higher among the pregnant women.

Recurrences.—It is apparent that the longer one continues the observation of a group of treated patients the more accurate will be the results of permanent cures. On the other hand, it is desirable to determine for any particular form of treatment that period of time after which recurrences may be considered improbable.

In general a six months' period of negativity as suggested by Davis,[9] appears to be a reliable indication of a permanent cure for any method of treatment.

The present study indicates that a period of negativity of eight weeks after a series of 6 treatments with aldarsone, administered in accordance with the technic described gives reasonable assurance of a permanent cure, when confirmed by repeated microscopic examinations.

PRINCIPLES IN TECHNIC OF TREATMENT

Although the vagina is the seat of active multiplication of the trichomonads, small numbers of organisms can frequently be recovered from surrounding structures. Bland and Rakoff[4] have emphasized the importance of routinely treating the cervix, the urethra, the vestibule, and external genitalia, in addition to the vagina.

In the technic which we have described the entire lower genital tract is thoroughly cleansed with some mild antiseptic solution, with the purpose of mechanically removing most of the secretion and preparing the mucosa for further medication. The drying which follows the initial cleansing is an important part of the technic. In the group of patients reported this was accomplished by repeated tamponing with pledgets of soft absorbent cotton. More recently, at the suggestion of Dr. T. L. Montgomery we have used a current of warm air from a modified hair drier with much satisfaction.

We have repeatedly found occasional organisms in the secretion within the cervical canal. Although active multiplication of organisms does not appear to take place within this structure, organisms from this source may initiate a recurrence when conditions within the vagina again become suitable. On this basis tincture of metaphen

was routinely introduced into the cervical canal on cotton applicators. This preparation was found to be a good trichomonadicide and could be dried quickly.

Ackermann[1] noted trichomonads in the urethra of a number of patients who had repeated recurrences. Treatment of the urethra in addition to the vagina facilitated the cure of these patients. In a number of the present group of patients plugs of secretion containing trichomonads were recovered from the urinary meatus. An aqueous solution of metaphen 1:500 was therefore routinely instilled in the urethra and also carried into the paraurethral recesses.

SUMMARY

1. Laboratory and clinical investigations were conducted to determine the efficacy of a new soluble pentavalent arsenical, aldarsone (sodium-methylene-sulphon-amino-hydroxy-phenyl-arsonate) in the treatment of trichomonas vaginitis. The results were compared with those obtained with acetarsone.

2. Studies in vitro indicated that aldarsone has a definite trichomonadicidal power, which is many times that of acetarsone. The trichomonadicidal power of aldarsone was not inhibited by human blood serum.

3. One hundred women with trichomonas vaginitis were treated by the insufflation of 0.5 gm. of aldarsone, diluted with kaolin, following preliminary cleansing of the vagina and vulva with a diluted tincture of green soap and water, instillation of tincture of metaphen into the cervix, and an aqueous solution of metaphen 1:500 into the urethra. A total of 91 women remained free from trichomonas during a period of three to nine months following treatment. Of these 84 women who remained negative after a series of 6 treatments, 5 required an additional series of 6 treatments, and 2 were cured after 2 additional series of treatments.

4. Of 25 women treated by a similar technic with acetarsone, only 12 or 44.4 per cent remained free from trichomonas, while 13 had repeated recurrences.

5. It is concluded that clinical experience as well as laboratory studies indicate that aldarsone is much superior to acetarsone in the treatment of trichomonas vaginitis.

6. Approximately three-fourths of the women treated were gravid. The results of treatment among the pregnant group with both acetarsone and aldarsone were slightly better than among the nongravid group.

7. Among a total of 36 recurrences which were noted following treatment with aldarsone 22 were detected during the first two weeks following treatment, while none were noted either clinically or by microscopic study after eight weeks.

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1621 Spruce Street.

MANAGEMENT OF SECONDARY AMENORRHEA OF FUNCTIONAL ORIGIN

Abraham B. Tamis, M.D., New York, N. Y.

(From the Department of Laboratories and Gynecological Endocrine Clinic of Lebanon Hospital)

SECONDARY amenorrhea of functional origin remains a perplexing therapeutic problem. Attempts to reestablish the menses by the use of gonadotropic and estrogenic substances alone have not proved to be a panacea for this disorder. Better results have been obtained by the use of thyroid extract and by x-ray "stimulation" of the ovaries and pituitary gland. Pelvic massage, dilatation of the cervix, dietetic regimes, and oral preparations of various internal secretory glands have also appeared to be effective in "curing" amenorrhea.

One conclusion which may be drawn from the use of such varied therapeutic measures is that the mechanism of menstruation, while essentially controlled by the anterior pituitary gland and the ovaries, is not absolutely independent of other influences, which may be endocrine, physical, or even psychic in origin. This being true, better results should be obtained if the specific physiologic disturbance in any individual case could be ascertained in advance of treatment, and then to apply the therapeutic agent found most suitable for the particular disorder. It is unreasonable to expect estrogenic hormone to be as effective in amenorrhea due to hypothyroidism as it is in underfunction of the

ovaries. Likewise it is superfluous to use gonadotropic hormone in instances of ovarian failure since this substance is already present in excess in these cases.

To prevent misapplication of useful therapeutic agents, R. T. Frank et al.[1] advocated a specific routine procedure in the study of functional amenorrhea as a basis for the rational interpretation of its etiology and cure. The report which follows is predicated on a similar routine, with results warranting a more detailed analysis.

Since 1933, twenty-five cases of functional amenorrhea were observed at the Gynecological Endocrine Clinic of Lebanon Hospital. With few exceptions, these women had received one or more unsuccessful courses of treatment prior to registration at the clinic, including the use of pills, hypodermic medication of ovarian and pituitary sex hormones, and x-ray "stimulation" of the pituitary gland and the ovaries. As a whole, these patients typified the more severe forms of secondary amenorrhea. Their ages ranged from seventeen to thirty-six years, the average age being twenty-five years. All of the women in this series had menstruated prior to the onset of amenorrhea. Eighteen patients complained of absent menstruation for periods of six months to three years. Seven patients were amenorrheic for less than six, but more than three months. Each case was carefully studied to exclude non-functional causes of amenorrhea, arising from pathologic states of the genital organs, from nutritional disorders, or from tuberculosis. A basal metabolism and an analysis of the urine for gonadotropic and estrogenic hormones were then performed. The clinical and laboratory data when completed were analyzed for etiologic leads upon which to base the treatment. The method of therapy was adapted to each case. Menstruation was restored, and the regularity of the menstrual cycles greatly improved in 60 per cent of the patients.

Patients with diminished uterine bleeding but regular cycles, and those whose menstrual intervals never exceeded two months, were not included in this study as these women become easily adjusted to their irregularity and seek professional advice only when concerned about the presence of a pregnancy.

The question of most importance in any case of amenorrhea is whether the ovaries are functioning. This may be determined in three ways: by the history, by biopsy of the endometrium, and by hormonal analyses.

A history of cyclically recurrent low abdominal pains and breast pains similar to those which the patient had previously experienced with menstruation suggests the presence of some ovarian activity.[1] This was present in eight patients, all of whom proved to have ovarian function on hormonal analyses (Table I). The demonstration of a "premenstrual" or "secretory" type of endometrium by curettement not only indicates ovarian function but also demonstrates a proper

balance in the elaboration of follicular and lutein hormones. Biopsy of the endometrium by means of the suction curette-cannula* I have devised can be performed in the office with very little discomfort to the patient. Finally, ovarian activity may be detected by analyses of the blood or the urine for estrogenic and gonadotropic substances. On the basis of the analyses, it is possible to determine not only the presence of ovarian activity but also whether the follicular function of the ovaries is normal or diminished.

Another essential factor to be determined in a case of secondary amenorrhea is whether ovarian function has ceased completely. If the

TABLE I. SYMPTOMATOLOGY OF AMENORRHEIC PATIENTS

CASE	AGE	PELVIC PAIN	BREAST PAIN	FLUSHES	DURATION OF AMENORRHEA
Group 1—With Normal Follicular Function					
1	21	Absent	Absent	Absent	10 months
2	23	Absent	Absent	Absent	3½ months
7	22	Absent	Absent	Absent	3 months
8	24	Present	Present	Absent	10 months
9	29	Present	Absent	Absent	3 months
11	23	Present	Present	Absent	3 months
15	31	Absent	Absent	Present	3 months
19	28	Absent	Absent	Absent	12 months
Group 2—With Diminished Follicular Function					
4	27	Absent	Present	Absent	3 years
5	28	Present	Absent	Present	6 months
12	17	Absent	Absent	Absent	11 months
13	25	Absent	Absent	Absent	5 months
14	29	Absent	Absent	Absent	3 years
17	18	Absent	Absent	Absent	5 months
18	19	Present	Absent	Absent	6 months
20	19	Absent	Absent	Absent	10 months
21	18	Absent	Absent	Absent	4½ months
23	25	Present	Absent	Present	8 months
24	36	Absent	Absent	Present	1 year
25	30	Absent	Present	Absent	2 years
Group 3—With Ovarian Failure					
3	34	Absent	Absent	Present	6 months
6	31	Absent	Absent	Present	8 months
10	32	Absent	Absent	Present	10 months
16	29	Absent	Absent	Present	13 months
22	17	Absent	Absent	Absent	9 months

menopausal state exists, obviously therapeutic efforts are bound to fail even though uterine bleeding may be restored by substitution therapy. Here again the history, type of endometrium, and hormonal analyses give valuable information.

A history of "hot flushes" and prolonged amenorrhea is generally interpreted as a menopausal manifestation. Eight patients had these symptoms (Table I). Four were found to exhibit some follicular activity and two of them, Cases 5 and 15, both young women, subsequently reestablished their menstrual cycles. The other four patients

*Manufactured by the American Cystoscope Makers, Inc., New York City.

were proved, by hormonal analyses, to have an early climacterium. Therefore, unless the "flushes" are associated with definite hormonal changes indicating complete cessation of ovarian function, no significance can be attached to its presence.

The finding of marked genital atrophy, in the form of ill-defined labia, conical and narrow vagina, and small uterus, also gives no index of the ovarian function. Advanced cases of genital atrophy were found among women with normal follicular activity as well as those with diminished or absent gonadal function. Menstruation was restored or improved in four of the twelve patients with genital atrophy. One patient, Case 25, later became pregnant, thus indicating the extent to which the reproductive mechanism may recover.

The demonstration of a "resting" endometrium by curettement does not preclude ovarian activity even if obtained on two or more successive weekly examinations. At most it signifies an inadequate production of estrogenic hormone.

TABLE II. ESTROGENIC FUNCTION OF OVARIES AS DETERMINED BY HORMONE ANALYSIS OF THE URINE

Group 1	Estrin present in normal or excessive amounts Prolan-A absent or occasionally present	Normal follicular function
Group 2	Estrin present in small amounts Prolan-A absent or occasionally present	Diminished follicular function
Group 3	Estrin absent Prolan-A absent or occasionally present	Diminished follicular function
Group 4	Estrin absent Prolan-A persistently present	Ovarian failure

The best method of ascertaining complete failure of ovarian function is by means of hormonal analyses of the blood and/or the urine. At menopause an excess of prolan A, the gonadotropic hormone elaborated by the anterior pituitary gland, can be demonstrated in the circulating blood.[2] It is also present after complete extirpation of both ovaries or after radiation castration. Other investigators have shown that prolan is consistently present in the urine under similar circumstances.

From the foregoing, it is clear that hormonal analyses gives the most reliable index of the status of the estrogenic function of the ovaries. Therefore it should be an essential step in the study of amenorrhea. This was performed in every case in this study, and repeated at various intervals after treatment to detect any changes. Unfortunately the relation of progestin to amenorrhea was not studied because the method of identifying this lutein hormone, that of Allen,[3] is too expensive and time-consuming for a routine laboratory procedure.

The method of hormonal analysis adopted was that advocated by Kurzrok and Ratner.[4] Each patient brought a full twenty-four-hour collection of urine once weekly for four consecutive weeks. The specimens were measured and divided into two portions, one of which was

tested for prolan and the other for estrin. The details of the extraction and hormonal identification followed by the author are adequately described in a previous communication.[5]

The hormonal reactions obtained are grouped in Table II, and are similar to those described earlier by Kurzrok.[6] Similar groupings have also been described by Frank[7] both in the blood and in the urine.

TABLE III. ENDOCRINE TYPES WITH SECONDARY AMENORRHEA

1. Hypothyroidism	a—with obesity b—with low basal metabolism
2. Hypopituitary obesity	
3. Hypoovarian obesity	
4. Eunuchoidism	
5. Eumorphic females	a—with normal follicular function b—with diminished follicular function c—with ovarian failure

According to Smith and Smith,[8] the method used in this study extracts only about 60 per cent of the total amount of estrin present. Therefore the failure to demonstrate estrogenic hormone does not absolutely exclude its presence in small amounts. For that reason, Groups 2 and 3 should be considered as a single group with Group 3 representing the severer grade of dysfunction.

Having established the state of ovarian activity, it is equally essential to seek for evidences of other glandular disturbances. The prepituitary lobe and the ovaries, though the principal regulators of the menstrual cycle, are in turn influenced by other organs of the endocrine system, particularly the thyroid, the adrenals, and even the pineal gland. Furthermore, it is known that psychogenic and neurogenic disturbances may alter menstrual activity. Therefore it is necessary to determine the basal metabolism, and to note any alterations in weight, hirsuitism, character of the skin, anthropometric variations, enlargement of the thyroid, and size of the breasts, all of which are directly or indirectly controlled through the activity of the endocrine system. The physical variations may be sufficiently pronounced to permit of a fairly accurate diagnosis of the gland at fault. Thus we have learned to distinguish clinically the hyperthyroid, the hypothyroid, the Frölich syndrome, and so forth. This differentiation, however, is not always possible and not often recognized unless carefully noted.

On the basis of the physical examination and the laboratory criteria, the patients in this study could be appropriately reclassified into the endocrine types shown in Table III. This classification served as a working basis for therapy and proved to be most helpful from a prognostic standpoint. A more detailed description of the cases is tabulated in Tables IV and V.

Patients Evidencing Hypothyroidism with Obesity (3 cases).—

These three patients not only exhibited the rather typical shoulder deposition of fat, but also thickening of the dermis, dryness and loss of hair, and lassitude.

TABLE IV. SECONDARY AMENORRHEA

CASE	AGE	DURATION AMENORRHEA	OVER-WEIGHT	BASAL METAB.	GENITAL ATROPHY	SIZE OF BREASTS	HORMONE		THERAPY	RESULTS
							ESTRIN	PROLAN		
		1a—Cases With Hypothyroid Obesity								
1	21	10 months M = 12 × 4 - 6 mo. × 7	+39	?	Moderate	Normal	+ +	0	Diet + thyroid	Bled 2 wk. later. Then reg. every month for 2½ years
8	24	10 months M = 14 × 30 d × 4 → D + C	+37	+ 7	Moderate	Normal	+ +	0	Diet	Lost 15 pounds → menses ensued → pregnant → quite reg. since
20	19	10 months M = 16 × 3 - 9 mo. × 4	+38	-10	Marked	Normal	+	0	Thyroid	Bled every 1½ to 2 mo. during the next 2 years
		1b—Cases With Low Basal Metabolism								
7	22	3 months M = 14 × 3 - 6 mo. × 4	-3	-27	None	Normal	+ +	0	Thyroid	Bled every 1-3 months during next 3 years
13	25	5 months M = 14 × 2 - 3 mo. × 5	-4	-13	None	Atrophic	+	0	Thyroid	Bled every 1-2 months during next 8 months
23	25	8 months M = 12 × 28 d × 2	+8	-15	None	Normal	0	0	"Stim" x-ray of ovaries	No improvement
10	32	10 months M = 14 × 24 d × 4	0	-20	Marked	Atrophic	0	+	"S" x-ray ov. "D" x-ray pituit.	No improvement
		2—Cases With Hypopituitary Obesity								
2	23	3½ months M = 12 × 1½ - 3 mo. × 5	+44	-6	Marked	Pendulous	+ +	0	Thyroid	No improvement
24	36	1 year M = 13 × 1 - 3 mo. to 1922 then amen. 6 yr.,	+34	-1	Marked	Pendulous	0	0	Follutein + amniotin	No return of menstruation. Menstrual symptoms +
6	31	8 months 1 yr. M = 13 × 28 d × 3	+66	?	Marked	Pendulous	0	+	Thyroid	No improvement
		3—Cases With Hypoovarian Obesity								
11	23	3 months M = 13 × 28 d × 5 to 1921 then every 3 - 12 mo.	+23	-7	Marked	Normal	+ +	0	Follutein + amniotin	Bled every 1-2 months during next 3 years
21	18	4½ months M = 14 × 3 - 9 mo. × 4	+24	-7	None	Normal	+	0	"Stim" x-ray of ovaries	Bled every month during next 2½ years
		4—Eunuchoidism								
12	17	11 months M = 15 × 1 - 2 mo. × 5	-8	-4	Marked	Normal	0	0	Foll. + amniot. thyroid "S" x-ray ov.	No improvement

TABLE V. EUMORPHIC FEMALES

CASE	AGE	DURATION AMENORRHEA	OVER-WEIGHT	GENITAL ATROPHY	SIZE OF BREASTS	THERAPY	RESULTS
			a—Normal Ovarian Estrogenic Function				
9	29	3 months M = 14 × 2 - 10 mo. × 4	+18	None	Normal	None	Bled every 1-1½ mo. following examination
15	31	3 months M = 13 × 30 - 45 d × 8	0	None	Normal	None	Bled every 30-35 days following examination
19	28	12 months M = 15 × 28 d × 4 → 26 yr. then every 1-3 mo.	+14	Marked	Atrophic	Refused	No improvement
			b—Diminished Ovarian Estrogenic Function				
4	27	6 months M = 11 × 28 d × 4	- 6	None	Normal	"Stim" x-ray of ovaries	No improvement
5	28	6 months M = 12 × 28 d × 8	- 2	Moderate	Normal	Dilatation of cervix	Bled every 28 days following treatment
14	29	3 years M = 13 × 28 d × 4 → 21 yr. then every 1½-3 mo.	+ 8	Marked	Normal	Follutein + amniotin	No return of menstruation. Menstrual symptoms +
17	18	5 months M = 16 × 3 mo. × 5	0	Marked	Normal	Follutein + amniotin	Bled every 1 to 1½ months during next 3 years
18	19	6 months M = 12 × 1-3 mo. × 5, then menorrhagia 1½ yr.	-14	None	Normal	"Stim" x-ray of ovaries	Bled regularly q 28 d. for 5 mo. → menorrhagia
25	30	2 years Only menses 2 yr. ago	- 5	Marked	Normal	"Stim" x-ray of ovaries	Bled once. Normal pregnancy followed. Menses regular
			c—Ovarian Failure				
3	34	6 months M = 11 × 28 d × 4	0	None	Atrophic	Refused	No improvement
16	29	13 months M = 13 × 28 d × 5	- 4	Marked	Atrophic	"Dep" x-ray of pituitary	No improvement
22	17	9 months M = 13 × 4-6 wk. × 4	+ 3	Marked	Atrophic	"Stim" x-ray of ovaries	Menses recurred—became regular after 8 months

Despite the prolonged period of amenorrhea (ten months), ovarian function was normal in two women and diminished in one. This was interpreted as indicating a hopeful prognosis. The patients were placed on a reducing diet and desiccated thyroid extract (Armour).

The patient in Case 1 began to menstruate regularly after taking thyroid for only two weeks, perhaps too soon to attribute the clinical cure to the use of the drug. Incidentally this woman, two years previously, established menstrual regularity for several months, after a twelve-month period of amenorrhea, merely by losing 40 pounds in weight. The amenorrhea recurred with the return of her adiposity. Frank has emphasized this relationship between obesity and amenorrhea before.[1]

The patient in Case 8 began to menstruate after a loss of 15 pounds and became pregnant six months later. A reduction in weight accomplished by dieting alone (thyroid tolerance poor) apparently aided in her cure.

Case 20 failed to lose weight but menstruated more frequently as long as she remained on thyroid medication.

Patients Evidencing Hypothyroidism without Obesity (4 cases).—These patients presented no evidence of diminished thyroid activity other than a low basal metabolism. The rates varied from -13 to -27. Mussey and Haines[10] reported 27 similar cases of amenorrhea associated with low basal metabolism, none of whom presented any organic disease to which to attribute the lack of bleeding.

Patients in Cases 7 and 13 received thyroid medication and shortly thereafter showed distinct clinical improvement.

The patient in Case 23 was a severe diabetic. Thyroid extract was withheld lest it might influence the glucose tolerance and thus interfere with the administration of insulin. She was reluctant to try any hypodermic medication, so that x-ray "stimulation" of the ovaries* was resorted to. Menstruation, however, failed to ensue. Further hormonal analyses likewise revealed no improvement.

Case 10 was the only patient with hypothyroidism whose ovarian function, as determined by hormonal analyses, had ceased completely. Thyroid therapy proved unsuccessful. This is not surprising in view of the poor prognosis indicated by the hormonal findings.

Of the seven patients with hypothyroidism, five were clinically improved. The prognosis in this type of patient is much better than in any of the other endocrine types. It is with good reason therefore, that Novak was led to conclude that "thyroid extract still remains as the sheet anchor in the treatment of functional amenorrhea."[11]

Patients with Hypopituitary Obesity (3 cases).—These patients had pendulous breasts, large abdominal aprons of fat, and were from 34 to 66 pounds overweight. They also presented an acromegalic facies.

The patient in Case 2 was found to have normal follicular function of the ovaries. Basal metabolism was -6. Her tolerance for thyroid extract, even in small doses, was poor. Despite all dietary control she continued to gain weight. The menstrual intervals, which formerly lasted three months, now lengthened to six months.

The patient, Case 24, before coming under my observation, had been treated with extracts of the thyroid gland and ovaries. and also by irradiation of the pituitary gland and the ovaries without any beneficial results. Hormonal analyses of the urine revealed no estrin or prolan (Group 3 reaction, Table 2). Accordingly, these substances were given three times weekly for several weeks in the form of amniotin† and follutein.† However, menstruation did not ensue. It is interesting

*The technic of x-ray therapy was performed under the direction of Dr. C. L. Okralnetz of the Radiotherapy Department, Montefiore Hospital, New York City.

†These preparations were generously donated by E. R. Squibbs and Sons through Dr. J. J. Durrett. The amniotin assayed at 50 R.U. per c.c. and the follutein at 100 R.U. per c.c.

to note that following the injections, the patient experienced low abdominal pains and tingling of the breasts, symptoms which did not exist prior to treatment. After treatment was discontinued, these symptoms failed to recur. This clinical response to hormonal therapy probably represents a gonadal reaction, and as such, is a helpful prognostic sign. The failure to initiate uterine bleeding in this patient may have been due to insufficient dosage of the hormones.

The third patient, Case 6, showed complete ovarian failure on hormonal analyses. She failed to respond to treatment, which was expected.

Patients with Hypoovarian Obesity (2 cases).—The obesity in these two patients was somewhat generalized but predominated about the thighs and hips. There were no changes in the hair or skin. The breasts were normal.

Although the follicular hormonal excretion of Case 11 reached normal values, most of the specimens examined gave subnormal amounts. For that reason, the patient was placed on amniotin (450 R.U.) and follutein (300 R.U.) weekly for three months. Subsequently the menstrual cycles recurred every one to two months instead of from three- to twelve-month intervals. The improvement in menstruation was accompanied by a marked improvement in the function of the ovaries, demonstrated by further hormonal analyses.

The other patient in this group, Case 21, was treated similarly but the treatment had to be discontinued because of allergic manifestations following the injections of amniotin. She was also intolerant of small doses of thyroid extract. As a last resort, a "stimulating" dose of x-ray was given to both ovaries. Menstruation set in four weeks later, and since then has recurred every one to one and one-half months instead of the former three to nine-month intervals. Hormonal analyses showed corresponding improvement in ovarian function.

Eunuchoidism (1 case).—Berkow[12] described several cases of eunuchoidism with amenorrhea. These patients were of normal mental and physical development, except for a hypoplasia of the genital tract and a disproportion of bony growth, the extremities being relatively too long for the trunk. The growth disturbance is due to a lack of ovarian influence on the ossification centers of the long bones during early adult life. The hypofunction of the ovaries is in turn due to a deficiency of the gonadotropic function of the anterior pituitary lobe.

Case 12 was of this type. Hormonal analyses revealed no excretion of follicular hormone. Treatment with amniotin, follutein, thyroid extract, and "stimulating" doses of x-ray to the ovaries were of no avail. On one occasion, after receiving a total of 2,000 R.U. of amniotin in oil in ten days, the patient excreted follicular hormone for the first time. This was found to be exogenous hormone, because when treatment was discontinued no further estrin could be demonstrated. This patient has been observed for three years. The amenorrhea has persisted. Otherwise she has continued to enjoy excellent health.

According to Frank,[13] the prognosis in this type of female is poor but by no means hopeless, as clinical improvement may occasionally occur.

Eumorphic Females with Normal Basal Metabolism (12 cases).—These patients represented the normal type of female, being of average weight, with normal basal metabolic rates, and exhibited no stigmas of endocrine dysfunction other than the menstrual disturbance. Although clinically they constituted one complete group, hormonal analyses indicated a pronounced difference in their estrogenic function. To facilitate discussion, they are subdivided as follows:

A. Cases exhibiting normal follicular function
B. Cases exhibiting diminished follicular function
C. Cases exhibiting complete ovarian failure

Cases Exhibiting Normal Follicular Function (3 cases).—Two patients, Cases 9 and 15, menstruated spontaneously following their first visit to the clinic and

continued their cycles with greater regularity thereafter. The explanation for this is not clear in either instance. Anspach and Hoffman[14] reported spontaneous cures of some cases of amenorrhea by pelvic massage. They attribute the beneficial results to a disruption of atretic follicles, retention cysts, and persistent corpora lutea which are impediments to egg-ripening and ovulation.

The third patient, Case 19, had previously been treated unsuccessfully with various pills as well as radiation of the pituitary gland and the ovaries. Analyses of the urine revealed normal quantities of follicular hormone. Unfortunately, she was too discouraged by former failures to cooperate intelligently. Consequently no treatment was given at the clinic. She was last seen in July, 1935, with an amenorrhea of three years' duration. Hormonal analyses showed the ovaries to be still functioning, but at a lower level.

Cases Exhibiting Diminished Follicular Function (6 cases).—Menstrual function was improved in four of the six patients in this group.

The patient in Case 5 menstruated for two days following a biopsy of the endometrium. This was neither traumatic bleeding nor blood from a hematometra, because there was a slight delay in its appearance after the biopsy, and because the bloody fluid was typically menstrual in character. Subsequently she continued to menstruate regularly. It is interesting to note that the biopsy material failed to show a "premenstrual" mucosa. Possibly the uterine bleeding in this case is of the "anovulatory" type described by Novak.[15] Further studies on this subject are being made.

The patient in Case 17 had previously received thyroid extract without any beneficial effect. Treatment with estrogenic and gonadotropic hormones was instituted, a total of 1700 R.U. of amniotin and 1500 R.U. of follutein being given in three months. Following this, the menstrual intervals diminished from three-month intervals to cycles of one and one-half months. Hormonal analyses revealed a distinct improvement of the estrogenic function months after treatment had been discontinued.

Case 18, a single girl of nineteen years, originally came under observation because of menometrorrhagia. The bleeding stopped spontaneously and then became amenorrheic for six months. At first a pregnancy was suspected and apparently confirmed by the presence of a softened uterus and a positive Friedman pregnancy test. However, the uterus failed to enlarge and a second pregnancy test was negative. On this basis a diagnosis of a persistent lutein cyst was made, and x-ray "stimulation" of the ovaries was given. Shortly after this therapy, menstruation recurred and remained regular for several months. Lately the menorrhagia has returned, probably because of further cystic change in the ovaries.

The patient in Case 25 also received x-ray "stimulation" of the ovaries and immediately afterward menstruated. This was the first menstrual flow in two years. Hormonal analyses revealed a greatly improved ovarian function. When the next period failed to materialize, she was found to be pregnant and eventually was delivered of a normal full-term infant. Menstruation then recurred regularly for several months, only to be again interrupted by another amenorrheic interval due to a second pregnancy.

X-ray "stimulation" to the ovaries was tried unsuccessfully on patient in Case 4. Glandular therapy was advised prior to this but refused by the patient.

Patient in Case 14 was given 5,200 R.U. of amniotin and 10,000 R.U. of follutein over a period of five months with no menstrual response. Hormonal analyses, performed during intervals when she was free of treatment, revealed 3.5 to 6.6 R.U. of estrin (normal amount varies from 10 to 20 R.U.) where previously none could be demonstrated. This, in itself, indicated a distinct improvement in ovarian function. It is possible that, had larger doses of amniotin been given, such as are now available, a better result might have been obtained.

Cases Exhibiting Complete Ovarian Failure (3 cases).—This group was interpreted as typifying early menopause because of the similarity of the hormone findings to those present during natural or artificially induced menopause.

Two of the patients, aged twenty-nine and thirty-four years, respectively, were already experiencing "menopausal flushes." The older woman, Case 3, was content to know that menstruation would not recur and refused any treatment. The other patient, Case 16, received "depressive" doses of x-ray to the pituitary region with the hope that prolan production would be diminished. However, no clinical or hormonal changes were noted. Her "flushes," amenorrhea, and hormonal findings continued unabated.

The remaining patient in this group, Case 22, was a young girl of seventeen, who became amenorrheic immediately following an appendicectomy. Whether the operation was an etiologic factor in producing the menstrual dysfunction is difficult to say. It is also hard to believe that the ovaries of so young a girl should have exhausted all primordial follicles unless we assume that there existed a congenital deficiency of such structures. It was more rational to assume that some inhibitory force was present which prevented the proper cyclical development of the primordial follicles. Such a factor might well be a persistent lutein cyst, as this body is known to inhibit maturation of the follicles. The excess of prolan was interpreted as an attempt on the part of the anterior pituitary gland to reactivate the ovaries.

From a therapeutic standpoint, it is obviously wrong to give this patient additional gonadotropic substance. Patients with complete ovarian failure have much larger quantites of this hormone circulating in their blood than may be administered hypodermically. Follicular hormone in large amounts may induce an artificial flow but it is mere substitution therapy. The uterine bleeding resulting therefrom will cease after discontinuing therapy. No stimulating effect on the ovaries will take place.[16]

The only remaining agent which might prove of value to such a case is the x-ray. So-called "stimulating" doses were given to the ovaries and menstruation followed two weeks later. Hormonal analyses of the urine then revealed the presence of subnormal amounts of estrin but no diminution in the content of prolan A. After two menstrual periods, the amenorrhea recurred. Another course of x-ray "stimulation" was given. The patient then began to experience the molimen at monthly intervals, but actual bleeding did not take place until eight months later. Since then, she has menstruated regularly each month, and recent hormonal analyses revealed normal quantities of follicular hormone. However, prolan A excretion was still present in every specimen. This prognosticates a probable recurrence of the amenorrhea.

DISCUSSION

The pituitary-ovarian control of menstruation has been generally accepted, though much remains to be clarified. This control is affected in many endocrinopathic disorders and accounts for the frequent association of obesity with amenorrhea.[1] The keen observer will recognize differences in the fat deposition, depending upon the gland or glands at fault.[9] Alterations in bony growth, and in the character of the skin and skin appendages will frequently be noted in any large series of long-standing secondary amenorrheic patients. A low basal metabolism is commonly present.

Unfortunately the physical examination alone gives no inkling of the ovarian function. Two individuals, seemingly alike physically, may differ considerably in regard to their gonadal activity. Many failures

in therapy are attributable to this difference. It is most advisable, in patients with prolonged amenorrhea, to perform an analysis of the blood and/or the urine for estrogenic and gonadotropic hormones. This information readily reveals the degree of ovarian follicular activity or inactivity. It yields tangible evidence upon which to base a prognosis. Hormonal analysis is unnecessary where the amenorrheic intervals are of short duration.

From a therapeutic standpoint, desiccated thyroid extract and x-ray "stimulation" of the ovaries proved to be the best agents in restoring menstruation in this series of cases. They accounted for two-thirds of the cures.

The part played by the thyroid gland in inducing menstruation is not fully understood. The stimulating effect on the ovaries may be brought about indirectly through stimulation of the anterior pituitary lobe, and directly by the power of thyroxine to increase cellular activity generally. When the ovarian function is normal in the presence of a coexisting hypothyroidism, as in Cases 1 and 7, the manner of action of thyroid extract is not quite clear. Possibly the bleeding results from some alteration in the endometrium. This is merely a suggestion. As a matter of fact, despite all the theories pertaining to the mechanism of menstruation, the actual cause of the menstrual flow, the so-called "bleeding factor," is as yet unknown. Until this is more clearly understood, the basis for thyroid therapy must rest on theoretical considerations only.

Thyroid extract is not always well tolerated, even in small doses. The patients must be frequently re-examined for signs of thyroid intoxication, and the basal metabolism rechecked. The amount used was the largest dose tolerated by the patient without producing toxic symptoms. As a rule, it ranged between 3 and 6 gr. of thyroid extract (Armour) daily.

It is erroneous to speak of x-ray irradiation as a "stimulating" agent. It is always a destructive force. When "stimulating" effects follow its use, it is due to the destruction of some inhibitory force. This was shown experimentally by Van Pée and Simon.[17] They irradiated the ovaries of mature rabbits and dogs, and demonstrated a selective sensitivity of the various structures in the ovaries to the rays. The most sensitive was found to be the maturing follicle, and the least sensitive to be the corpus luteum, due in all likelihood to the less mature and more actively growing granulosa cells of the follicle.

Whether this effect of x-ray on animal ovaries is equally true of human ovaries is not known, although clinical observations indicate it to be so. Cystic ovaries have long been known to cause delay in menstruation. The removal of these cysts by partial oophorectomy or by puncture has been followed by the re-establishment of menstruation.

The destruction of similar cystic structures by the x-ray might explain the "stimulating" effect of irradiation obtained in Cases 18 and 22.

Rongy,[18] in 1927, was the first in this country to describe the beneficial influence of x-ray "stimulation" in secondary amenorrhea. Since then several reports have appeared substantiating these results, the latest being that of Mazer and Spitz.[19] These authors stress the fact that x-ray should be a measure of last resort because of the possibility of inducing castration atrophy despite the control of dosage.

The hope that the newer ovarian and prepituitary sex hormones would prove as effective for amenorrhea as insulin is for diabetes mellitus, or thyroxine for hypothyroidism, has not been fulfilled. This is due to the fact that, in most instances, the amenorrhea exists as a symptom and not as a disease entity. It is often part of a pluriglandular syndrome involving more than one specific hormone.

Estrogenic and gonadotropic hormones should be used primarily in cases exhibiting diminished ovarian function. Patients with ovarian failure (menopause-like states) are not proper subjects for glandular therapy and attempts to cure them with the sex hormones are misapplications of useful therapeutic agents.

Amniotin and follutein were given to six patients, all of whom were demonstrated to have poor ovarian follicular activity. Menstruation was re-established with greater regularity in two (Cases 11 and 17). One woman, Case 14, exhibited an improved follicular function of the ovaries but failed to menstruate. Another, Case 24, experienced the molimina while under treatment, but the hormonal findings and the amenorrhea continued unchanged. Case 21 was allergic to amniotin, a contraindication for continuing this treatment. The sixth patient, Case 12, failed to respond in any manner to hormonal therapy.

Since this study was begun, the strength of amniotin has been increased to 400 R.U./c.c. and to 2,000 R.U./c.c., an improvement that more nearly approximates the amount necessary to build a proliferative endometrium in the human uterus. Kaufmann[20] showed that 25,000 to 50,000 R.U. of estrogenic hormone per month, reinforced by 25 to 50 rabbit units of progestin (corpus luteum hormone) were required to induce true menstruation in human castrates or postclimacteric women. With functioning ovaries, less of the follicular and lutein hormones is needed, but the dosage for any individual case can be determined only by trial and error.

The future for hormone therapy was best expressed by R. T. Frank[21] who stated that "the prospect that eventually hormone therapy of gynecologic and obstetric functional disturbances will be put on a rational and effective basis is excellent. Such result will develop from well-selected, carefully controlled and objectively studied series of cases; perhaps by trial and error, certainly not by machine gun type of endocrine drugging to which the profession is becoming addicted."

CONCLUSIONS

1. A series of 25 cases of secondary amenorrhea of functional origin are reported. Most of these cases had failed to respond to the usual therapeutic measures before presenting themselves for study. Menstruation was restored and the regularity of the menstrual cycles greatly improved in 60 per cent of these patients.

2. The patients were classified according to their endocrine type and to the status of their ovarian function. This was determined by noting physical stigmas of endocrine dysfunction, by the basal metabolic rate, and by hormonal analyses of the urine for estrogenic and gonadotropic hormones.

3. The prognosis for restoration of menstruation was best in those women with normal ovarian function, and poorest in those with ovarian failure.

4. The treatment regime, in any individual case, depended upon the group to which the patient conformed.

5. The procedures effective in the highest percentage of cases were desiccated thyroid extract (Armour) and x-ray "stimulation" of the ovaries. Next in effectiveness were amniotin (Squibbs) and follutein (Squibbs).

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1882 Grand Concourse

Beilby, Julius H.: Persistent Headache During Lactation, Brit. M. J. 2: 337, 1935.

A few cases are reported of persistent headache associated with the nursing period, which characteristically disappeared on weaning. No underlying cause was discoverable in any of the cases. The condition is rare and is most likely to occur in multiparas. It is usually seen in those of very poor economic circumstances and poorer physical condition, where nursing is an added burden. Dental caries is often an associated but not a causative factor. Rigid prenatal care and improvement of the general condition during the puerperium are essential in treatment. Weaning is the final therapeutic measure, if the symptoms justify it.

F. L. Adair and S. A. Pearl.

THE CELL VOLUME FOLLOWING DELIVERY AND ITS RELATION TO BLOOD LOSS AND POSTPARTUM INFECTION*

JOHN B. PASTORE, M.D., NEW YORK, N. Y.

(From the Department of Obstetrics and Gynecology, Cornell University Medical College and the New York Hospital)

IN A RECENT study of the third stage of labor by the author, it was demonstrated that the incidence of puerperal infection was proportional to the blood loss. The reduction of infection, therefore, involves not only the elimination of the factors during pregnancy, labor, and delivery, which influence the blood loss, but also the proper treatment of the patient who has sustained a hemorrhage.

There are two factors which are definitely established at the present time. First, the blood loss increases with the weight of the patient, and second, the seriousness of the hemorrhage is inversely proportional to the body weight, for example, a patient weighing 90 kg. will tolerate a loss of 1,000 c.c. much better than the patient weighing only 50 kg. Since we also know that the blood volume is proportional to the body weight, we have expressed the blood loss as a percentage of the weight of the patient. Thus:

$$\frac{\text{Blood Loss (c.c.)} \times 100}{\text{Wt. of Pat. (Kg.)} \times 1000} = \frac{\text{Blood Loss (c.c.)}}{\text{Wt. (Kg.)} \times 10} = \text{Per cent Blood Loss.}$$

For example, if the blood loss was 260 c.c. and the weight of the patient 65 kg., the percentage of blood loss would be $\frac{260 \text{ c.c.}}{65 \text{ kg.} \times 10} = 0.4$ per cent. Most of our patients are weighed before and after delivery, and the weight before delivery was used in this calculation. Where this was not obtained the last weight in the prenatal course was used. By this method, a blood loss of 600 c.c. would be 1.0 per cent in the average patient weighing 60 kg. and would therefore be considered a hemorrhage, whereas it would be only a 0.66 per cent loss for a patient weighing 90 kg. On this basis, the percentage of loss is much more valuable than the actual loss in cubic centimeters.

Determining the incidence of postpartum infection on this basis, we have the graph as represented in Fig. 1. This includes all patients who had a rise in temperature to 38° C. or more during two twenty-four-hour periods and excluding the first twenty-four hours after delivery. The graph represents the incidence of infection in 1,431 cases of premature and full-term vaginal deliveries which were discharged from the hospital between May 1, 1935, and Feb. 1, 1936. The blood loss was measured by the method described in an earlier publication.[7]

*Presented before the Section of Obstetrics and Gynecology, Buffalo Academy of Medicine, April 15, 1936.

Ninety-two per cent of all the patients with vaginal deliveries during this period are included in Fig. 1. In the other 8 per cent of the cases, including deliveries on the isolation floor which is not equipped with a measuring apparatus, the blood loss was not measured for various reasons.

For blood losses less than 0.3 per cent, the incidence of infection remains fairly constant around 6.5 per cent. Above this value it rises rapidly until the blood loss reaches 0.7 per cent. This initial rise increases the incidence of infection by over 100 per cent. For losses between 0.7 per cent and 1.0 per cent the incidence of infection is again constant. A secondary rise begins at the hemorrhage range,

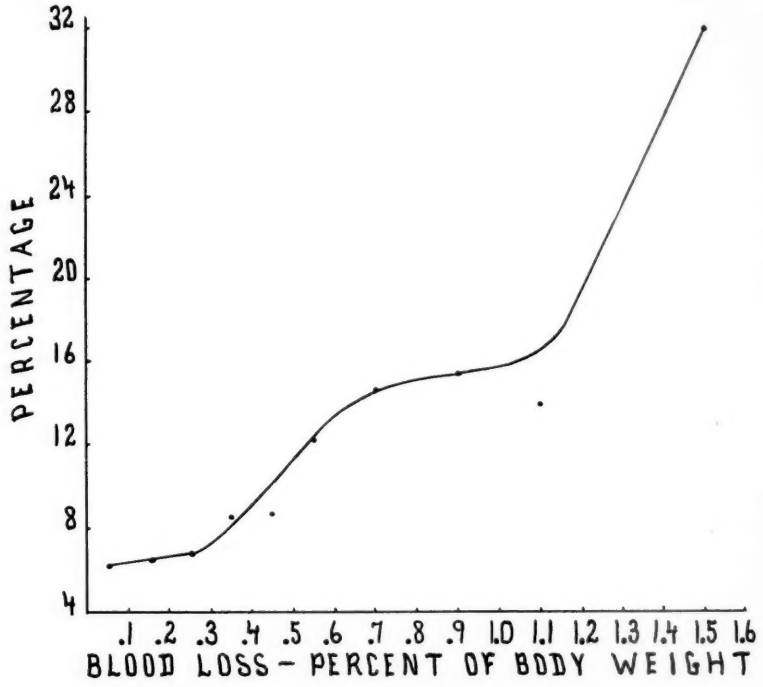

Fig. 1.—Showing relation of postpartum infection to the blood loss during the third stage of labor.

1.0 per cent blood loss, and increases the incidence to 31.8 per cent for an average blood loss of 1.5 per cent. This rise is represented as a straight line, although it should probably be a line parallel to the first rise. This is due to the fact that there were only 44 patients with a loss of over 1.1 per cent, and this number was too small to subdivide into individual groups.

It then became desirable to know if this increase in infection had any relation to the change in hemoglobin and cell volume following delivery, and if we could establish a method whereby we could predict the change in cell volume following a known blood loss. It had

been planned to follow the hemoglobin and the cell volume before delivery and during the puerperium. The Sahli method was used for the determination of hemoglobin, but in spite of the fact that all the determinations were done by me under controlled conditions, variations as high as 10 per cent were often noted on the same blood. This error is particularly noticeable when the determinations are made by different individuals, including students and internes. For clinical purposes it did not seem practicable to do the determinations by the oxygen method of Van Slyke. The studies have therefore been restricted to the cell volume determinations as outlined by Wintrobe. About 3 c.c. of blood were obtained by venipuncture, and to this two drops of heparin were added. To avoid congestion, the tourniquet was always removed before any of the blood was withdrawn. About 200 of the venipunctures were done by four members of the house staff of the Woman's Clinic, and the remaining 700 by me. All of the determinations were personally conducted. One cubic centimeter of blood was placed in a Wintrobe tube and centrifuged for one hour. The tubes were then allowed to stand for several minutes to regain room temperature, and the layer of white blood cells was disregarded in reading the cell volume. A total of 928 determinations were made.

The cell volume was studied before delivery and during the puerperium in 240 normal patients and in 48 with toxemia of pregnancy. In addition, cell volume studies of 31 other patients with antepartum toxemia, including vomiting of pregnancy, and cesarean sections, were made. Except for the cases of cesarean sections, the study of this small group was made only during the antenatal course. The third postpartum day was found most suitable for comparative studies, since the maximum drop in cell volume was usually attained by that day. The cell volume late in the puerperium was not constant because of the presence of infection in some of the patients. Most of the readings before delivery were obtained early in labor.

It was noticed in this investigation that the cases of toxemia, particularly those due to eclampsia and preeclampsia, deviated markedly from the normal course. Dieckmann in 1933 and Skajaa in 1929 made the same observation, although they did not correlate the changes with the blood loss. For this reason, in correlating the cell volume changes with the blood loss only the normal cases are considered.

Fig. 2 represents graphically the relation of the cell volume on the third postpartum day to the various groups of blood loss. The cell volume is expressed as a percentage of its value before delivery; for example, if the cell volume was 40 per cent before delivery and it dropped to 32 per cent on the third day, it was expressed as 80 per cent, indicating that there had been a 20 per cent drop in the cell volume. This method was employed in order to standardize all the changes. Obviously, comparison of absolute figures would be misleading, since all of the patients

did not have the same cell volume before delivery. It can be seen from the graph that the cell volume on the third day is higher than it was before delivery when the blood loss does not exceed 0.3 per cent. The graph is almost a straight line for losses up to 0.7 per cent. The cell volume change then remains constant between 0.7 per cent and 1.1 per cent blood loss. Beyond this range the drop in cell

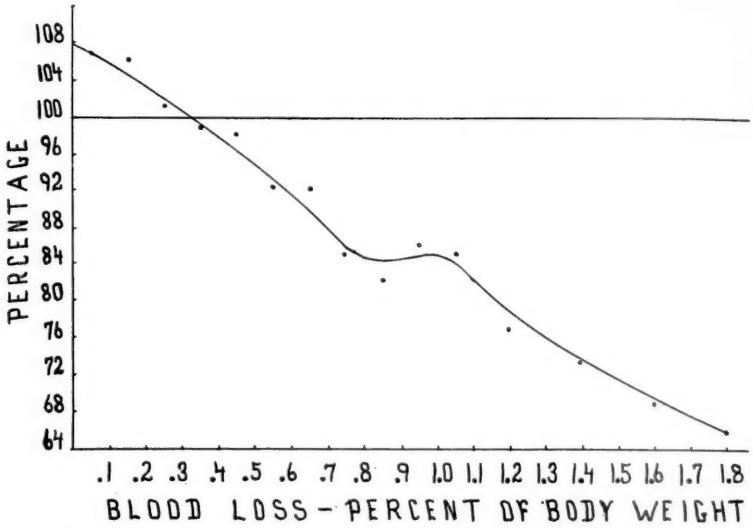

Fig. 2.—Showing relation of cell volume on the third postpartum day to the blood loss during the third stage of labor.

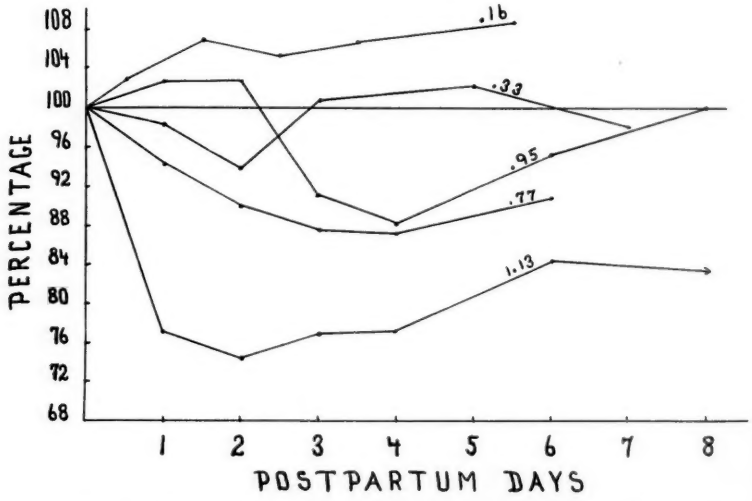

Fig. 3.—The course of the cell volume during the puerperium.

volume is almost parallel to the initial change. Here again the number of cases in the higher groups of blood loss is small. The range in cell volume, the average figure, and the number of cases in each group are given in Table I.

In Fig. 3 the course of the cell volume in the puerperium in 5 cases with different blood losses is represented. A discussion of these curves will be presented later.

DISCUSSION

The lowest incidence of postpartum infection is found in the group of patients with a blood loss of less than 0.3 per cent. In comparing Fig. 1 and Fig. 2, we find that within this range of blood loss there is an increase in cell volume by the third postpartum day. Such a rise in cell volume seems to be necessary for an ideal puerperium, since most of the patients who have an absolutely afebrile course, that is, with variations of not more than 0.2° C. above the normal, fall into this group of blood loss. With larger blood losses, in spite of the fact that the puerperium is considered afebrile, fluctuations in temperature

TABLE I. CELL VOLUME ON THE THIRD POSTPARTUM DAY WITH THE VARIOUS BLOOD LOSS GROUPS. CELL VOLUME IS EXPRESSED AS A PERCENTAGE OF THE VALUE BEFORE DELIVERY

PER CENT BLOOD LOSS	CASES	CELL VOLUME	
		RANGE	AVERAGE
Less than 0.1	27	99-119%	107.0%
0.1 to 0.2	44	92-121	106.3
0.2 to 0.3	36	87-113	101.2
0.3 to 0.4	40	89-108	99.0
0.4 to 0.5	19	80-110	98.2
0.5 to 0.6	18	80-108	92.1
0.6 to 0.7	16	77-100	91.3
0.7 to 0.8	12	83- 90	85.4
0.8 to 0.9	4	80- 86	82.0
0.9 to 1.0	9	72- 93	86.0
1.0 to 1.1	4	77- 94	85.4
1.1 to 1.3	4	69- 84	77.0
1.3 to 1.5	4	61- 81	73.6
1.5 to 1.7	3	62- 73	68.4
1.8	1		66.0

between 37° and 38° C. are usually noted. These we have been calling low-grade fevers although the temperature never reached 38° C.

This increase in cell volume must be due to dehydration of the blood following delivery, as has been recently shown by Oberst and Plass. Although an actual decrease in the total blood volume in the puerperium has not been clearly demonstrated, we do know, from the work of Plass and Bogert, Stander and Tyler, Stander and Creadick, Miller, Keith, and Rowntree, Dieckmann and Wegner, and many others, that there is dilution of the blood during pregnancy. Compensation for this dilution must occur after delivery or during labor. The amount of dehydration during the first three days of the puerperium is equivalent to 0.3 per cent of the body weight, since it is at this point that the dilution due to blood loss and the dehydration following delivery, are balanced. Furthermore, if this is true, we would expect that the drop in cell volume at 0.6 per cent blood loss should be the same as the rise at 0.0 per cent. From Fig. 2 it can be seen that this statement is correct, since the change in cell volume in each case is approximately 8 per cent.

Why should the incidence of infection between 0.7 and 1.1 per cent blood loss remain fairly constant? If there is any correlation between infection and cell volume, then the drop in cell volume within this range should also remain constant. Such a finding is demonstrated in Fig. 2. The only explanation which I can offer for this finding is that the bone marrow may perhaps be stimulated when the blood loss exceeds 0.7 per cent of the body weight. Apparently the maximum stimulation is obtained at 1.1 per cent since the drop in cell volume beyond this loss is parallel to the original drop. Although the blood from these patients was not studied for evidence of regeneration, we did note that the cell volume increased more rapidly in the cases with 0.9 per cent blood loss than in those with 0.7 per cent loss. Careful study of the blood and even of the bone marrow will be necessary to substantiate this conclusion.

In studying these cases on the basis of absolute values for the cell volume, it was found that in all patients who had a cell volume of 40 per cent or over on the third postpartum day, the incidence of infection was 4.5 per cent; in those who had a cell volume between 30 and 40 per cent, the incidence was 7.5 per cent and in those whose cell volume dropped below 30 per cent, the incidence of infection increased to 31.0 per cent. Furthermore, in the 19 cases of postpartum hemorrhage, which we have defined as a blood loss of 1.0 per cent or more of the body weight before delivery, there were 7 cases in which the cell volume was 30 per cent or over on the third day. Only one of these had a febrile course. In the other 12 cases the cell volume dropped below 30 per cent, and 6 or one-half of these patients had a febrile puerperium. The remaining 6 had a low-grade fever. The possibility that the low cell volume was due to the infection is ruled out, because the determinations were made at the time when the infection was nonexistent or just beginning. From this we can conclude that the absolute value of the cell volume is of importance.

What then should be our treatment in these cases? If the incidence of infection follows the cell volume curve, it would seem that our treatment should be directed toward maintaining as high a level of cell volume as is possible, not only during pregnancy but particularly after delivery. Medications are not useful after delivery since their action is slow. Transfusion is the only method which gives us a prompt replacement. Obviously we do not feel that transfusions are necessary in all cases of hemorrhage, since the incidence of infection in this group is only 31.8 per cent. The usual tendency is to "wait and see what the hemoglobin does." However, it is possible to determine at the time of delivery what the course of the cell volume will be during the puerperium. Knowing the cell volume before delivery and the blood loss in terms of the body weight, we can calculate, from the graph in Fig. 2, what the cell volume on the third postpartum day

will be. If we find that this calculated cell volume is below 30 per cent, then that patient should receive a transfusion within the first twelve hours following delivery. This is true not only for the cases with hemorrhage, but also for all patients with a blood loss above 0.3 per cent. The amount of blood that should be given depends on the weight of the patient, the blood loss, and the cell volume before delivery. In the average patient of 60 kg., a transfusion of 500 c.c. is equivalent to 0.83 per cent of the body weight. Purely from the standpoint of blood loss, if a patient lost 1.5 per cent and received 0.8 per cent in the form of a transfusion, the uncompensated blood loss would be around 0.7 per cent. By reference to Fig. 1, we would expect an incidence of infection of 14 per cent in contrast to 31.8 per cent, or a decrease of over 50 per cent in that group. If the transfusion were large enough so that the uncompensated blood loss was around 0.3 per cent, then the incidence of infection would approach the base line of 6.5 per cent. If the cell volume is also taken into consideration, we can go one step further. Knowing the cell volume before delivery, we can calculate, from the graph in Fig. 2, the amount of blood which that patient can lose before her cell volume drops below 30 per cent. If a transfusion of 500 c.c. is enough to replace the difference between the actual blood loss and the above calculated loss, then we could expect to maintain the cell volume above 30 per cent. According to the findings reported above, our expected incidence of infection would be 7.5 per cent. Moreover, if the transfusion was large enough to maintain the cell volume above 40 per cent, the incidence of infection would be around 4.5 per cent. The amount of blood necessary in each case can be calculated from Fig. 2. A more composite chart is not presented because this has not yet been tested clinically. I have of course not taken into consideration the stimulating effect of a transfusion, the difference in cell volume of the bloods of the donor and recipient, and the possible destruction of some of the red blood cells. Moreover the period of hospitalization for these patients has not been considered. We know from a previous study that patients with postpartum hemorrhage remain in the hospital on an average of three to four days longer than the normal cases. Such a treatment, therefore, would be economical for the hospital, especially if a free donor is secured.

Although this study was undertaken primarily to determine the changes in cell volume in the normal cases, I did have the opportunity of observing a few cases of toxemia of pregnancy. When the blood loss is expressed in terms of the body weight, variations from the normal can be easily detected. In the eclamptic and preeclamptic patients the cell volume dropped out of all proportion to the blood loss. On the basis of this study, this finding would explain the higher incidence of infection in this group of patients. Also during the acute stage of the disease there was a marked increase in the cell volume, as

was observed by Dieckmann and Skajaa. There was, therefore, dehydration of the blood in spite of the fact that there was excessive fluid in the body tissues. This seems to explain why so many of these patients have fever during the acute stage. Eden and more recently Peckham have shown that the presence of fever is a poor prognostic sign, and on this basis the fever would be an expression of the degree of dehydration occurring in the blood. In the true nephritic patients the cell volume did not drop as much as in the normal cases. Of the few cases of low reserve kidney which I observed, some behaved like the nephritic type, others like the eclamptic, and still others like the normal cases as far as the cell volume was concerned. In these cases of toxemia the cell volume must be an expression of the changes in the blood volume. This is substantiated by the fact that in the cases of vomiting of pregnancy the cell volume was markedly increased, and with subsequent improvement it returned to normal. It followed the curve of the CO_2 of the blood in the reverse order. It will be interesting to follow the cell volume in the cases of vomiting of pregnancy which do not improve with the usual treatment.

If the cell volume is a good index of changes in the blood volume, then we should determine the normal curve throughout pregnancy. It is not sufficient to know that the cell volume during the middle of pregnancy is lower than in the nonpregnant woman, or even at term. The normal curve of pregnancy, expressed in terms of percentage change, would be valuable in detecting early those cases which deviate from the normal, particularly the toxemias of pregnancy. Since eclampsia is associated only with pregnancy, it must be an expression of abnormal physiology, and until we know what the normal is, it will be difficult to determine the cause of the disease.

Another possibility along these lines is shown in Fig. 3, which represents the changes in cell volume during the puerperium in 5 cases with different blood losses. In two of these, 0.33 per cent and 0.95 per cent, variations during the first two days can be seen. Whether these changes are due to poor fluid intake and output or to some form of toxemia cannot be definitely stated at this time. Such changes were noted quite frequently during this investigation. In both of these cases the antenatal course and the puerperium were clinically normal.

Recently Dieckmann and Daily have stated that the measurement of the total volume of blood lost at the time of delivery is misleading because of the concentration or dehydration of the blood during labor. They recommended that the blood loss be calculated from the amount of hemoglobin lost. This involves the accurate determination of hemoglobin, by the oxygen method of Van Slyke, of the blood at the time of delivery and of the waste material on the drapes and floor. This method would be advisable if the concentration of the red blood cells were markedly increased. The slight difference in cell volume is more

than offset by the inability to collect all of the hemoglobin and also by the tremendous amount of work involved. In addition, such a method does not give any information regarding the blood loss during the three phases of the third stage or the course of the hemoglobin during the puerperium. These are of importance if we are to make any progress in the control and treatment of bleeding.

In this investigation the changes in cell volume during labor were usually slight, the marked changes occurring only in the cases of toxemia and of prolonged labor where dehydration was present. Moreover, if there is normal dehydration of the blood during labor it is only the beginning of the process which extends into the puerperium. If this is a constant finding, it should not interfere with the results which we are seeking, namely, Can the course of the patient during the puerperium be predicted at the time of delivery, so far as the cell volume and the possibility of infection are concerned? The preceding results have shown that this is possible if the weight of the patient, the cell volume early in labor, and the blood loss accurately measured are known.

CONCLUSIONS

1. The blood loss at the time of delivery should be expressed in terms of the body weight; that is, as a percentage of the weight before delivery. From a prognostic and comparative standpoint, this is much more valuable than the actual volume of blood lost.

2. On this basis a loss of 1.0 per cent or more is considered a postpartum hemorrhage.

3. The incidence of infection during the puerperium increases with an increase in blood loss. This increase varies with the blood loss as represented in Fig. 1.

4. The normal amount of dehydration of the blood during the first three days of the puerperium is equivalent to 0.3 per cent of the body weight.

5. The cell volume on the third postpartum day varies with the blood loss. It is higher than the value before delivery when the blood loss does not exceed 0.3 per cent of the body weight. With larger blood losses there is a drop in cell volume.

6. Stimulation of the bone marrow is probably obtained with losses greater than 0.7 per cent, with maximum stimulation at 1.1 per cent. This possibly accounts for the constant values in the incidence of infection and the change in cell volume within this range of blood loss.

7. The incidence of infection is also dependent on the cell volume on the third postpartum day. With a cell volume of less than 30 per cent, the incidence of infection is 31.0 per cent in contrast to 4.5 per cent when the cell volume is above 40 per cent.

8. The cell volume for the third postpartum day can be calculated at the time of delivery from the graph in Fig. 2. If this calculated cell volume is below 30 per cent, that patient should receive a transfusion within the first twelve hours following delivery. The amount of blood required depends on the weight of the patient, the blood loss, and the cell volume before delivery. This can also be calculated from Fig. 2.

9. In the toxemias of pregnancy the cell volume during the puerperium deviates from the normal course. The patients with eclampsia and preeclampsia have a greater drop in cell volume than is expected from the blood loss. The reverse is true in the nephritic patient. The low reserve kidney is not a pure type of toxemia as far as the cell volume is concerned.

10. The cell volume determination is a simple, accurate, and reliable procedure, and should be used more frequently in obstetrics.

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Bittmann, O.: The Justification of Special Anesthesia in Obstetrics, Monatschr. f. Geburtsh. u. Gynäk. **102:** 223, 1936.

The advantages of spinal anesthesia for operative obstetrics are as follows: Absolute insensitivity of the field of operation, complete relaxation of the lower uterine segment, diminished blood loss as the result of the action of spinal anesthesia in the contractility and retractility of the uterus, absence of worry on the part of the operator, no alteration in the vitality of the newborn babies, subjectively favorable influence on the puerperium, especially on the involution of the uterus, and therapeutically good results in eclampsia because convulsions diminish.

Among the disadvantages the author mentions the drop in blood pressure, which may be serious, especially where there has been a great loss of blood. The danger of severe atonic hemorrhage after the effect of the spinal anesthetic wears off may be prevented by the prophylactic injections of pituitary extract and ergot. Pituitary extract perhaps also diminishes the severity of the headache which often follows spinal anesthesia.

J. P. Greenhill.

TRAUMATIC GYNATRESIA

FRED A. KASSEBOHM, M.D., AND MILTON J. SCHREIBER, B.S., M.D.,
NEW YORK, N. Y.

(From the Obstetrical Service of the Harlem Hospital)

VAGINAL and uterine packing, invaluable and often irreplaceable in the control of postpartum bleeding, cannot be employed indiscriminately with impunity. Unquestionably a life-saving measure in certain situations, it is neither innocuous nor free of sequelae. In four years we have seen five cases of irreparable vaginal atresia, each traceable, we believe, to a common etiologic factor; the packing of a lacerated, abraded vagina with iodoform gauze. In the same period we were twice forced to cesarean section in multiparas in whom we had anticipated easy, spontaneous delivery, by almost complete failure of cervical effacement and absolute default of dilatation of the external os. Again, a common etiologic agent was found; electrocoagulation of the endocervical mucosa for chronic endocervicitis.

The iodoform gauze used on our service is prepared by the resident nursing staff. In the preparation, under aseptic precautions, it is attempted to impregnate gauze packing with an emulsion of iodoform in glycerin. This is done manually and the usual product is entirely satisfactory. On occasion, an uneven distribution of iodoform occurs, often concentrated in palpable masses in the gauze, which may be the cause of actual burns of the vaginal musoca. Such packing in the vagina abraded and lacerated by prolonged, traumatic delivery aggravates the already irritated area. When the packing is removed, the acutely inflamed mucosa, demonstrating early healing processes and possibly scattered bullae and blebs due to iodoform burns, collapses with the vaginal walls. The mucosae of the vaginal vault and floor and the lateral walls become contiguous. Sloughing at one area and healing at another may be concomitant and with ultimate healing, dense, fibrotic adhesions and areas suggestive of keloid formation unite the mucosae, producing atresia. Unfortunately this process occurs over the entire vaginal mucosa, and the atresia produced extends almost from the vulvovaginal orifice to the cervix. It is the distribution of the adhesive process throughout the vaginal canal that renders the resultant atresia resistant to treatment. Out of justice to the manufacturers of commercially available iodoform packing, it must be stated here that we have never seen atresia of any degree result from the usage of their packing; extensive experience indicates that there is no danger of atresia associated with properly prepared iodoform gauze. Where such is not available, it would be the course of wisdom to use plain packing

or, where the added advantage of antisepsis is desired, plain packing soaked in 4 per cent aqueous mercurochrome. This latter method was instituted on our service after the first four cases of atresia were encountered. A lapse in the procedure resulted in the fifth case. In the three-year period during which mercurochrome soaked packing was used no difficulty was seen.

The five cases, briefly described below, were seen in the postpartum clinic six to eight weeks following discharge from the hospital. Four of the five presented well-organized atresias at that time; dyspareunia was the chief complaint and with it vaginal bleeding following intercourse. No patient would accept hospitalization for treatment. The fifth patient had no complaint, the atresia being noted during the routine vaginal examination. She, too, refused therapy.

CASE 1.—M. M., para 0, colored, housewife, aged thirty-three, delivered with difficulty by Kielland forceps after prolonged arrest in midpelvis. Uterus and vagina were packed with iodoform gauze to control brisk postpartum bleeding. The perineum was intact. Birth weight of the baby was 8 pounds 8 ounces. The packing was removed forty-eight hours after delivery. She was discharged twelve days later in good condition. Delivery occurred on April 8, 1933. In the last week in May, vaginal atresia was observed at the postpartum clinic. Hospitalization was refused. On July 7, 1933, she returned complaining of dyspareunia, bleeding following coitus, and amenorrhea. In addition she stated that when she expected the period severe abdominal cramps had occurred and persisted three days. She was referred to the Gynecological Service where colpotomy was performed to relieve hematocolpos and hematometra. Dilatation of the vagina was attempted with glass dilators without satisfactory result. The patient signed herself out of the hospital and never returned for further treatment.

CASE 2.—J. O., aged thirty-two, colored, housewife, para iii, was admitted in active labor on March 23, 1932. Labor was rapid. A vertex presented and the interne on service had no difficulty delivering the head. Impaction of the shoulders occurred and ultimate delivery was effected by decapitation and cleidotomy (bilateral). Decapitation was deemed essential to permit proper and easier completion of the subsequent procedure. The stillborn child weighed 12 pounds 8 ounces. Uterus and vagina were packed with some 15 yards of iodoform gauze. Packing remained in situ for forty-eight hours. The patient had an uneventful puerperium and was discharged in good condition twelve days postpartum. In the first week in May, 1932, the examiner in the postpartum clinic noted the presence of an extensive atretic process in the vagina which prevented palpation of the cervix or fundus. On May 27 the patient was hospitalized complaining of dyspareunia, vaginal bleeding following coitus, and a persistent, bloody, vaginal discharge. The Gynecological Service attempted dilatation of the atresia with glass dilators but again prolonged treatment was refused.

CASE 3.—A. M., aged nineteen, white, unmarried. This patient delivered herself of a 7-pound 8-ounce stillborn child. After severe postpartum hemorrhage she was brought to the hospital by ambulance. On admission she was almost exsanguinated. The placenta was still within the uterus. After transfusion of 750 c.c. of whole blood, manual removal was performed, and the uterus and vagina were packed with iodoform gauze. Delivery took place on Nov. 13, 1932. In January, 1933 atresia was noted during routine postpartum examination. On March 30, 1933, the patient was hospitalized with the chief complaint of abdominal cramps and

dysmenorrhea. She was referred to the Gynecological Service where dilatation of the vagina was attempted with glass dilators, following manual dilatation of the vagina under anesthesia. She was discharged ten days postoperative and returned regularly for dilatation. On June 18, 1933, she was again hospitalized. The atresia had reestablished and the vagina was even narrower than on the occasion of the first admission. A plastic operative procedure was attempted with this admission, its purpose being to excise scar tissue and mobilize sufficient vaginal mucosa to recover the excised zones. The operative results were entirely unsatisfactory. The patient made several return visits for vaginal dilatation and then dropped out of the clinic.

CASE 4.—S. M., aged forty, colored, housewife, para iii, was delivered on Nov. 19, 1932, by Kielland forceps after failure of an occiput posterior to rotate anteriorly. A 9-pound 10-ounce baby was delivered. Profuse postpartum bleeding was controlled with iodoform packing of uterus and vagina. Packing was removed in forty-eight hours, and the patient was discharged in good condition ten days later. Twelve weeks following discharge she returned to the postpartum clinic where atresia was noted. At that time she was having a regular menstrual period. In December of 1933 she returned for examination. She was complaining of dyspareunia, amenorrhea, and severe, lower abdominal cramps.. She noted that the cramps occurred only on the dates of expected menses. Vaginal examination was impossible, the atresia being present at the vulvovaginal orifice and extending to the cervix. Per rectum, a large, boggy, cystic mass was noted. She was referred to the Gynecological Service where colpotomy was performed to relieve the hematocolpos and hematometra. Postoperative dilatation of the atresia was attempted without success.

CASE 5.—J. C., aged thirty-nine years, colored, housewife, para xi, diabetic, delivered on Feb. 9, 1936. Tranverse arrest occurred and delivery was effected with Kielland forceps. Impaction of the shoulders complicated delivery. An episiotomy was performed and a 12-pound 4-ounce baby delivered. Iodoform packing was placed in the uterus and vagina to control bleeding. The patient was discharged twelve days postpartum in excellent condition. On April 15, during routine postpartum examination, atresia of the vagina was noted. Vaginal examination was impossible since the atresia completely closed the vagina 1 cm. from the vulvovaginal orifice. The patient had no complaint. She was having a slight, bloody vaginal discharge. Inspection of the vagina revealed a complete closure of the orifice by what appeared to be normal mucosa. Close to the upper limit of the occluding membrane was an opening about 3 mm. in diameter through which the discharge could be seen escaping. She was referred to Gynecology where dilatation of the vagina was instituted.

Of these 5 patients, 2 complained of dyspareunia, 2 of dysmenorrhea, and 1 had no complaint. In 2, atresia was extensive enough to produce hematocolpos and hematometra. Therapy was eminently unsuccessful, and unless nature will permit gradual dilatation, these patients will never have functionally effective vaginas. The end-result in each of these cases favorably compares with similar results after expert management of the LeFort procedure.

In 1933, on two occasions, multiparas were admitted to the service in active labor; clinic cases, they had been thoroughly studied. Their prenatal courses had been normal, their pelves were ample, and from their histories and the adjudged size of the babies, no difficulty was anticipated. On admission, house men considered both fully dilated,

but it was noted that at no point, on rectal examination, was the margin of the cervix palpable. On vaginal examination, the presenting vertex was found to be covered by a smooth, elastic tissue presenting no opening. Inspection of the vagina with the speculum revealed a smooth, normal-appearing mucosa and no sign of cervix or external os. From the history of menstruation previous to pregnancy, we knew that a patent cervical canal must have been present. These 2 patients stated that they had been treated for profuse vaginal discharge by "burning out the neck of the womb." Records indicated that both had received electrocoagulation of the endocervix for chronic endocervicitis.

The bipolar electrode used in cervical coagulation is so constructed that, unless it is rotated while the current passes through it, coagulation will occur only at two points in the cervical canal. Where coagulation is performed with the electrode fixed in one position stenosis does not occur. Where the entire mucosa is destroyed at one sitting, slough and subsequent healing may completely close the canal or partially stenose it. Such stenosis is caused by the proliferation of dense, fibrous tissue which is undilatable. To prevent this accident one of two courses may be chosen. First, endocervical coagulation may be performed in two stages; second, after a one stage coagulation, or better, after any coagulation, uterine sounds should be gently passed through the cervix on several occasions and the patient should be instructed to report for examination after the first two menstrual periods have appeared. Dilatation gently performed with the sound will prevent stenosis, and unless the occluding pathology appears within two months, it will not appear.

These seven cases are presented to demonstrate the fact that dangers and associated sequelae are attached to apparently innocuous and beneficial procedures. The cure of endocervicitis is no justification for the risk of enforced cesarean section. Preventable iodoform burns of the vagina may be the starting point of prolonged physical, functional and psychic invalidism.

272 West 90th Street

509 West 155th Street

Robecchi, Emilio: Tubal Occlusion in Feminine Sterility, Ginecologia (Torino) 4: 463, 1936.

Based on the results of 180 hysterosalpingographies on women with primary or secondary sterility, the author stresses the high frequency of tubal occlusion in these patients.

Surgery offers very little assistance in reestablishing the patency of the tubes, but hysterosalpingography in itself occasionally causes occluded tubes to become patent and therefore proves useful at least in this respect.

August F. Daro.

PARENTAL AGE DIFFERENCE AND THE CONCEPTION OF CONGENITALLY MALFORMED CHILDREN

A Study of 600 Families

Douglas P. Murphy, M.D., Philadelphia, Pa.

(From the Gynecean Hospital Institute of Gynecologic Research and the Department of Obstetrics and Gynecology, University of Pennsylvania)

IN FAMILIES giving rise to congenitally malformed children, there is observed not infrequently a wide difference in the ages of the parents. In view of our lack of knowledge regarding the factors which may predispose to the production of congenital defects, the question is sometimes raised as to whether this parental age difference may not be an etiologic factor.

During an investigation of a consecutive series of families, each of which possessed a congenitally malformed child, the ages of both parents were ascertained. These figures with control observations are presented, since they appear to throw some light upon the problem under discussion.

MATERIALS AND METHODS

To quote from a previous communication,* the material forming the basis for the present report was secured in the following manner:

There were found in the files of the Bureau of Vital Statistics, Department of Health of the State of Pennsylvania, 130,132 death certificates for stillborn and live-born individuals, who died in Philadelphia during the five years between Jan. 1, 1929 and Dec. 31, 1933. Each of these certificates was examined, and the data on those noting the existence of any congenital defect were transcribed to duplicate official forms; 1,476 such certificates were located.

The deceased individual was considered to have possessed a defect under either of two conditions: (1) If the defect involved the surface of the body, or (2) if internal, if its presence had been disclosed by either operation or necropsy. Diagnoses not conforming to these requirements were considered as not verified, and were excluded from further consideration. This reduced the total number of usable certificates to 890, or only 60 per cent of the original 1,476 certificates.

An attempt was made to interview the mother of each of the 890 deceased individuals, the visits being made in the summer of 1934 by three fourth-year medical students. A complete reproductive history was secured from each mother who could be located. The group forms a consecutive series. The defective children all died within a given geographic area and in a given period of time.

THE DATA

The ages of both parents were determined for a consecutive series of families in which 600 congenitally malformed children were born. These data are recorded

*Murphy, D. P., and Mazer, M.: J. A. M. A. 105: 849, 1935.

in Table I, with identical facts for 600 families, picked at random from the general population. The latter families were selected in the following manner: They were located through the medium of licenses on file in the Marriage License Bureau of the City of Philadelphia. The files of this Bureau for the years 1929 and 1933 inclusive, were inspected. The first 120 licenses issued during each of these years were examined, and the age differences of the applicants were noted. A few

TABLE I. AGE DIFFERENCE OF PARENTS

AGE DIFFERENCE IN YEARS	PARENTS			
	WITH DEFECTIVE CHILDREN		CONTROL	
	NUMBER	PER CENT	NUMBER	PER CENT
Reported	600	100.0	600	100.0
0- 5	436	72.7	420	70.0
6-10	112	18.6	123	20.5
Over 10	52	8.7	57	9.5

substitutions were made in the resulting 600 records in order to insure numbers of control colored and white families comparable to the ones forming the defective child group.

It is evident from a glance at Table I that the distributions of parental age differences, in the defect families and in the control families, are essentially identical. On the basis of these observations, it is concluded that parental age difference is not a factor in the production of congenitally malformed children.

A CRITICAL ANALYSIS OF THE FIRST 3,060 CASES DELIVERED AT THE BRONX HOSPITAL*

J. IRVING KUSHNER, M.A., M.D., NEW YORK, N. Y.
(From the Obstetric Service of The Bronx Hospital.)

THIS report representing 3,060 consecutive deliveries at the Bronx Hospital from July, 1932, through November, 1934, will add some proof to the theory that among the most important causes of the prevailing high mortality rate are unnecessary interference and lack of proper training of the obstetric attendant. One thousand of these cases are from the ward service and 2,060 from the private services. The class of patients cared for in the ward service varied from the extremely poor to the comfortable middle class. Most of these were Jews.

On the ward service the expectant mother is required to register with the antepartum clinic before the seventh month of gestation. She is seen at intervals of two weeks and in the last month of gravidity every week to the time of delivery. The antepartum care consists of a complete physical examination including blood pressure and urine examination, mensuration, hygienic and dietetic regulation. The appearance of signs of toxemia, blood dyscrasia and the like indicates more frequent observation in the regular clinic or a special clinic or, when necessary, hospitalization. During labor unnecessary examination and interference is eliminated, rectal examination instead of vaginal being used; and the work of the staff is carefully supervised. The private services observe a reasonable degree of proper prenatal care and no operations except low forceps can be done except under supervision.

*Read by invitation before the section of Obstetrics and Gynecology of the New York Academy of Medicine, January 28, 1936.

Of the 3,060 labors, operative delivery was done 730 times, a frequency of 23.9 per cent, with a neonatal and stillbirth mortality of 1.9 per cent for the total series and 9 per cent (58 in 730) for the operative cases; a maternal mortality of 0.3 per cent. It is of interest to note that of the 1,000 labors on the ward service, operative delivery was done 184 times, a frequency of 18.4 per cent with a neonatal and stillbirth mortality of 1.9 per cent for the total cases and 9.7 per cent for the operative cases and with only one maternal death (Table I).

On the private services the low forceps operation was done in the greater propotion of the cases as a prophylactic measure. If we deduct this group from the total operative incidence, there is an operative frequency of 14.1 per cent for the entire

TABLE I. OPERATIVE INCIDENCE, ENTIRE SERIES

OPERATION	TOTAL NO.		FREQUENCY PER CENT		MATERNAL DEATHS		INFANT DEATHS	
	WARD	PRIVATE	WARD	PRIVATE	WARD	PRIVATE	WARD	PRIVATE
Cesarean section	19	84	1.9	4.7		6	1	10
Low forceps	85	276	8.5	14.3			3	5
Midforceps	50	138	5.0	6.8	1	1	1	7
High forceps	1	3	0.1	0.1				2
Version	6	24	0.6	1.1			2	10
Breech extraction	18	26	2.1	3.9			6	9
Craniotomy	2	1					2	1
Totals	730		23.9%		8		59 = 1.9%	
Frequency for operative cases					1.1%		9%	

TABLE II A. VERSIONS

INDICATION	NO.	MORTALITY	
		MOTHER	BABY
Failure of forceps	10	0	4
Second of twins	9	0	5
Unengagement	6	0	1
Marginal previa	3	0	1
Transverse presentation	2	0	1
Totals	30	0	12

TABLE II B. BREECH

	NO.	MORTALITY		MACERATED	ANOMALIES	PREMATURE	ATELECTASIS	EXTRACTION
		MOTHER	BABY					
Spontaneous	69	0	2	2				
Extraction	44	0	15		3	1	1	10
Totals	113	0	17	2	3	1	1	10

series. Low forceps applications on the ward service were strictly limited to definite indications in the interest of mother or child. The greater number of low forceps operations was done in primigravida, the indications for which, in order of their frequency, were: (a) maternal distress and prolonged labor. (b) Fetal distress (character of fetal heart rate in addition to the mere appearance of meconium). (c) Cardiac complications. (d) Contracted outlet (rigid coccyx and outlet contractions in funnel pelvis).

The eight infant deaths in low forceps deliveries include two congenital anomalies, two neonatal deaths due to cerebral hemorrhage and four from unknown causes (all these cases were autopsied).

The 188 midforceps operations are divided into two groups: (a) head anterior at time of operation, 78, and (b) head in posterior or transverse arrest position, 110, The indications were strict and ran parallel to these for low forceps on the ward service.

There were two maternal deaths after forceps operations: (1) Hospital No. 37452, a primigravida who had a midforceps for fetal distress after 4½ hours of full dilatation, occiput anterior. She sustained a left cervical laceration which was re-

TABLE III. CESAREAN SECTIONS

INDICATION	NO.	TYPE OF OPERATION				MORTALITY	
		CLASSICAL	2 FLAP	LATZKO	PORRO	MOTHER	BABY
Contracted pelvis	60	20	33	5	2	4	2
Previous section	9	9					
Central placenta previa	8	8				2	2
Fetopelvic disproportion	7		1	6			1
"Ablatio"	6	3			3		6
Toxemia	3	3					
Complicating fibroids	3	2			1		
Cardiac disease	3	3					
Malposition	2		1	1			
Elective toxemia	2	2					
Totals	103	50	35	12	6	6	11

TABLE IV. POSTPARTUM HEMORRHAGE

CAUSE	NUMBER	TREATMENT	TRANSFUSION	MATERNAL DEATHS
Atony of uterus	3	Uterine packing	0	
Adherent placenta	1	Manual removal. Uterine packing	+	
Cervical lacerations	25	Cervical suture. Packing	+	1
Manual removal	1	Packing	+	

TABLE V. TOXEMIA OF PREGNANCY

TYPE	NUMBER	PREVIOUS TOXEMIA	DELIVERY		MATERNAL MORTALITY	BABY			
			SPONT.	OPERATIVE		PREMAT.	FULL TERM	LIVED	DIED
Eclampsia	1		1		0	1			1
Preeclampsia	12	1	9	3	0		12	12	
Nephritic toxemia	7		7		0	1	6	4	3
Unclassified	22		22		0	2	20	20	2
Total	42	1	39	3	0	4	38	36	6

Fetal Mortality 14%

paired. Cervix and vagina were packed and 1,000 c.c. of glucose infusion was given. After some time bleeding recurred and she died five and one-half hours after delivery after a further attempt to repair the cervix; and (2) Hospital No. 38209 in a primigravida who had a midforceps operation for ineffectual pains. Patient developed circulatory collapse and anuria and died in uremia four days later.

The eight infant deaths in the midforceps deliveries include six cases where the fetal heart was not heard before delivery; one baby that died of a bronchopneumonia ten days later; and one death due to cerebral hemorrhage.

The high forceps operation was done four times. In 1 case the patient had a borderline pelvis and an arrested O. T. Manual dilatation of a five-finger dilated cervix resulted in dislodgement of an engaged head, changing a midforceps to a high one. In the other 3 cases the operation was done for fetal distress on unengaged heads where versions were contraindicated. Two fetal deaths occurred in this group; one of these babies had a cerebral hemorrhage.

Internal podalic version and extraction was employed 30 times for the following indications: (a) failure of forceps in occiput posterior, 10; (b) second of twins, 9; (c) unengaged occiput with full dilatation, 6; (d) marginal placenta previa, 3; and (e) transverse presentation with prolapsed arm, 2. Here the fetal deaths included 5 premature babies (less than 3 pounds in weight); 4 full-term stillbirths after failure of Kielland forceps; 1 macerated fetus and 2 congenital anomalies (Table IIA) incompatible with life.

Breech presentation was encountered 113 times. The treatment was strictly conservative, allowing labor to proceed until the buttocks had passed through the vulvar orifice, from which point manual help by the operator completed the delivery. This we call spontaneous breech delivery. Any other procedure was termed a breech extraction. The latter was done 44 times, an incidence of 6 per cent in the entire series. In the spontaneous group there were two macerated fetuses. In the extraction group there were 15 fetal deaths: 3 anomalies, 1 premature, 1 neonatal death from partial atelectasis, and 10 deaths in all probability due to the extraction (Table IIB).

Cesarean section was resorted to 103 times, a frequency of 3.4 per cent. The indications were as follows: (a) contracted pelvis, 60; (b) previous sections, 9; (c) central placenta previa, 8; (d) fetopelvic disproportion, 7; (e) "ablatio," 6; (f) toxemia, 3; (g) complicating fibroids, 3; (h) cardiac disease, 3; (i) malposition, 2; (j) elective in toxemia, 2. All patients, except 5 in the previous section group, 6 in the "ablatio" group, and 3 in the cardiac group were allowed a trial labor. In all, the presenting part was unegaged at the time of operation. The classical operation was done 50 times, the two flap 33 times, the Latzko 12 times, and the Porro 6 times.

The Porro operation was done twice for placental apoplexy, once for an intrapartum infection, and the other three times for failure of uterus to contract following classical sections. One of these was complicated by intramural fibroids.

The Latzko procedure was done for potentially infected cases, with one fetal death and no maternal deaths. This has been reported elsewhere.

The six maternal deaths occurred as follows:

1. Hospital No. 35052. Primipara at term; central placenta previa; generally contracted pelvis. Classical section. Died on sixth postoperative day of sudden cardiac collapse. Stillbirth.

2. Hospital No. 40100. Primipara at term; central placenta previa. Classical section. Died on tenth postoperative day of peritonitis. Living baby.

3. Hospital No. 42845. Primipara at term; funnel pelvis, frank breech. Classical section. Died on sixth postoperative day from paralytic ileus. Living baby.

4. Hospital No. 43415. Primipara at term, contracted pelvis, nonengagement at end of twenty-four hours with membranes ruptured eight hours. Two flap section. Neonatal death. *Streptococcus hemolyticus* septicemia.

5. Hospital No. 44529. Primipara at term, flat rachitic pelvis. Intrapartum sepsis. Porro section. Autopsy: localized peritonitis. Living baby.

6. Hospital No. 47503. Primipara at term, flat pelvis, two flap section for nonengagement at end of thirty-six hours of ruptured membranes and eight hours of labor. Died of pneumonia. Living baby.

The 11 fetal deaths include 6 in mothers with ablatio (fetus already dead when section was done); 2 in mothers with placenta previa where fetal heart was lost be-

fore operation; 1 in a mother who died of the *Streptococcus hemolyticus* sepsis; 1 in a mother where a high forceps was attempted at home and later a Latzko section done in the interests of the mother, and one neonatal death from unknown causes (Table III).

Retained placenta occurred 18 times. All but three were removed manually within two hours after delivery because of continued bleeding. In three cases without bleeding the manual removal was done at the end of twenty-four to thirty hours because of a rise in maternal temperature.

Postpartum hemorrhage estimated at more than 500 c.c. followed the delivery of the placenta in 30 cases, which are grouped as in Table IV.

Included under the heading of toxemia of pregnancy (classification of Dr. Stander), are patients with symptoms of headache, dizziness, spots before the eyes, edema, as well as those symptom-free whose systolic blood pressure was above 140, or where albumin was present in the urine.

These cases are followed weekly in a special clinic where blood chemistry, kidney function tests, and eyeground examinations are made. They are seen postpartum by the same clinic personnel at the end of six weeks, one year, and two years, as to their ultimate outcome.

There were 42 cases of toxemia in the 1,000 ward cases. Because of lack of proper study the private cases are not included (Table V). More than 50 per cent of the cases fall into the so-called unclassified group which includes the low reserve kidney of Stander.

MATERNAL MORBIDITY

The standard of morbidity used in this group was a temperature of 100.4° F. (rectal temperature) on two occasions after the first day postpartum. There was a gross morbidity of 7.5 per cent. Among these there was a rise of temperature as a result of nonobstetric causes in 52 cases as follows: (a) upper respiratory infection, 30; (b) pyelitis, 14; (c) cholecystitis, 4; (d) acute thyroiditis, 1*; (e) toxic erythema, 3. This makes a net morbidity of 6.1 per cent.

MATERNAL MORTALITY

In this series of 3,060 cases there were 11 maternal deaths, a frequency of 0.3 per cent.

a. Hospital No. 37452. Primigravida who had a midforceps operation for fetal distress after four and one-half hours of full dilatation. In the extraction a left cervical laceration was sustained which was recognized and immediately repaired. Cervix and vagina were packed and a glucose infusion given. Bleeding recurred and she died five and one-half hours after delivery after a further attempt to repair the upper end of the cervical laceration and a transfusion.

b. Hospital No. 35052. Primipara at term; central placenta previa; generally contracted pelvis. Classical section. Died on sixth postoperative day of sudden cardiac collapse. Stillbirth.

c. Hospital No. 40100. Primipara at term; central placenta previa. Classical section. Died on tenth postoperative day of peritonitis. Living baby.

d. Hospital No. 42845. Primipara at term; funnel pelvis, frank breech. Classical section. Died on sixth postoperative day from paralytic ileus (probably peritonitis). Living baby.

e. Hospital No. 43415. Primipara at term, contracted pelvis, nonengagement at end of twenty-four hours with membranes ruptured eight hours. Two flap section. Neonatal death. *Streptococcus hemolyticus* septicemia.

f. Hospital No. 44529. Primipara at term, flat rachitic pelvis. Intrapartum sepsis. Porro section. Autopsy: localized peritonitis. Living baby.

g. Hospital No. 47503. Primipara at term, flat pelvis, two flap section for non-engagement at end of thirty-six hours of ruptured membranes and eight hours of labor. Died of pneumonia. Living baby.

h. Hospital No. 38209. Primigravida who had a midforceps operation done for ineffectual pains. Patient developed circulatory collapse and anuria and died in uremia.

i. Hospital No. 36582. Primigravida, normal spontaneous delivery, suddenly developed pulmonary edema thirty minutes prior to delivery and died shortly after.

j. Hospital No. 47100. Primigravida, normal spontaneous delivery, intrapartum influenza. Died of *B. influenza* sepsis.

k. Hospital No. 50532. Gravida iii, eclamptic, spontaneous delivery after Strogonoff treatment. Died twenty-one hours after onset of first convulsion.

INFANT MORTALITY

In this series there were 135 infant deaths, a mortality rate of 4.4 per cent, 32 were macerated fetuses and 8 were congenital anomalies, leaving a corrected mortality of 3.1 per cent. Of these, 51 were premature infants (i.e., less than three pounds), leaving a full-term corrected infant mortality of 1.4 per cent.

COMMENT

We have presented an analysis of a series of 3,060 cases treated conservatively; where the indications for operative intervention were carefully weighed. The only prophylactic form of obstetric procedure that was employed was the careful antepartum treatment accorded every patient and the closer watching and observation accorded to the particular patient showing abnormalities.

The use of the midforceps, as well as version and cesarean section for absolute indications only, resulted in an operative incidence of 23.9 per cent, a net maternal morbidity of 6.1 per cent, a maternal mortality of 0.3 per cent, and a corrected infant mortality of 3.1 per cent.

I wish to express my sincere thanks to Dr. Meyer Rosensohn, Attending Obstetrician at The Bronx Hospital, for his helpful suggestions and valuable criticisms in the preparation of this paper.

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215 East Gunhill Road

Schumacher, P. H.: The Effect of Antithyroid Substances on the Secretion of Milk, Monatschr. f. Geburtsh. u. Gynäk. **100**: 211, 1935.

In August, 1934, Küstner reported that he had been able to increase the flow in lactating women by giving them antithyroid substance in the form of thyroxin. He based this therapy on his observation that a decrease in the amount of milk followed the administration of thyroid preparations. Schumacher tried to verify these results but failed. He did not observe any increase in the flow of milk after the use of antithyroid preparations. This author believes that the best way to obtain an increased secretion of milk still is complete emptying of the breast by the act of nursing or with the aid of a suction pump. However, he hopes that good results will soon be obtained with the use of the lactation hormone of the hypophysis.

J. P. Greenhill.

INTERSTITIAL PREGNANCY*

Case With Early Rupture, Treated by Vaginal Operation

T. K. Reeves, M.D., F.A.C.S., Pittsburgh, Pa.
(From the Department of Gynecology, Pittsburgh Hospital)

THE interstitial portion of the uterine tube is the least common of all locations for the lodgment of tubal pregnancies. Based on the figures of Rosenthal and of Wynne, it appears to occur in no more than 1 or 2 per cent of all ectopic gestations.

The diagnosis of ectopic gestation at this site is almost impossible to make before rupture. Even after rupture it is seldom that it can be more than suspected of being in the uterine portion of the tube until exposed by operation.

The following case report is presented because of the comparative infrequency of the condition, the unusually early rupture in this instance, and the nature of the operation selected as being especially adapted to this type of case.

Mrs. M. C., a white woman, aged twenty-six years, married ten years, had three children, aged nine years, two and a half years, and eleven months, respectively. Each labor was spontaneous and the puerperia were uncomplicated.

Her last menstrual period began July 28, 1935 and ended Aug. 2, 1935, being normal in every respect. On Sept. 26, 1935, or seven weeks after her last period ended, the patient felt uncomfortable in her lower abdomen. Later, while working in her garden, she was suddenly seized with violent pain in the lower abdomen, became dizzy, and fainted. She recovered consciousness in not over five minutes and was able to crawl into the house but could not rise to her feet. After resting on the floor of her bathroom, she was able to rise and attempted ineffectually to defecate. She fainted again in the bathroom and was unconscious for approximately one hour. Finally, she was able to get to her bedroom and onto the bed, where her husband found her about two and one-half hours after the first attack. She was conscious at this time and refused to have a physician. There was no vaginal bleeding. At 9:00 P.M. she became unconscious again and a doctor was summoned who sent her to the hospital. The patient was admitted to the Pittsburgh Hospital at 10:00 P.M., semiconscious but in severe shock, with clammy skin and so weak a pulse that the rate could not be definitely determined. Her blood pressure was unreadable. The blood count disclosed 30 per cent hemoglobin and 1,900,000 red cells. The abdomen was distended and rigid and the vaginal examination was negative until the cervix was reached. This was lacerated, somewhat softened, and displaced anteriorly; slight movement of the cervix caused pain to the patient. The posterior fornix of the vagina was convex and bulging tensely. Uterus and adnexa could not be outlined. The diagnosis was ruptured ectopic gestation with severe hemorrhage.

The patient had been treated for shock by the usual methods and a 10 per cent acacia solution (500 c.c.) had been administered intravenously. The blood pressure still could not be recorded; 500 c.c. of whole blood were then given by the Soresi direct method followed by 1,000 c.c. of 10 per cent dextrose solution. Repeated attempts to read the blood pressure were made but no pulsation could be heard.

*Read before the Pittsburgh Obstetrical and Gynecological Society, April 6, 1936.

The patient's condition was so desperate that it was decided to attempt to clamp the bleeding vessels through the pelvic culdesac.

The patient was given nitrous oxide anesthesia, placed in a marked Trendelenburg position, the vagina prepared with iodine and a transverse incision approximately 2 cm. in length was made over the bulging area posterior to the cervix. When the peritoneum was opened, dark red blood and clots literally spurted out. The total amount was not determined. The index finger was introduced through the incision and the left adnexa was palpated. The tube and ovary on this side were normal in size and mobility. The right adnexa were next felt and also found to be normal but the right cornu of the uterus presented an opening into which the index finger could be introduced. It was now obvious that this was a ruptured interstitial pregnancy.

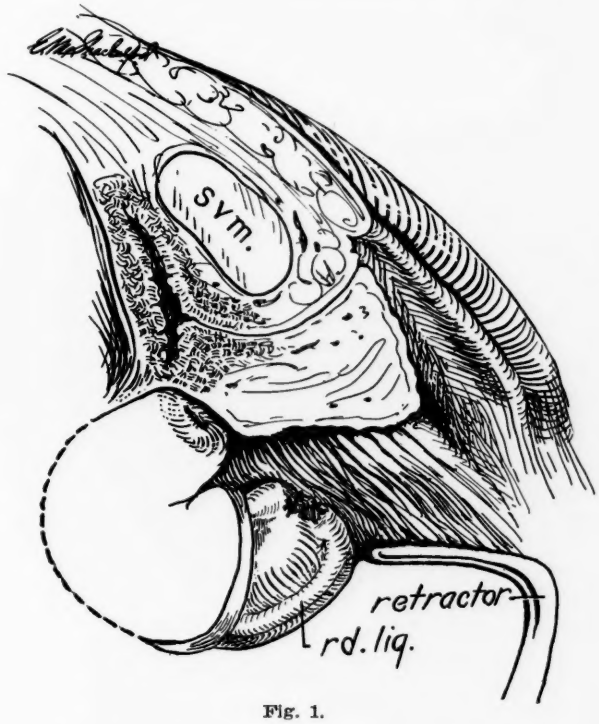

Fig. 1.

The uterus was displaced posteriorly and grasped with a tenaculum, the incision enlarged, and the uterus was drawn down and out through the vagina. The right cornu, approximately 1 cm. from the entrance of the tube, showed a horizontal tear about 2 cm. in length, the edges being very ragged, purple in color, and bleeding moderately. In the myometrium there were several grayish white areas which were removed for examination; fetal elements as such were not seen. The wound was quickly sutured, the uterus replaced, and three cigarette drains placed in the culdesac.

The time of anesthetic was twenty minutes and the time of operation twelve minutes.

During and following the operation, the patient was given 600 c.c. of whole blood and 1,500 c.c. of physiologic saline solution.

One-half hour after operation the blood pressure was 50, systolic, but the diastolic could not be determined. The pressure gradually rose until six hours later when it was 92/68, while the hemoglobin had become 50 per cent and the red blood cells had increased to 3,510,000.

The patient suffered a delirium on her second day and pulled out the drains. Subsequently she developed a pelvic abscess which necessitated reopening of the incision in the culdesac for drainage. She was discharged in good condition after sixty-one days in the hospital.

119 South Highland Avenue

EPITHELIOMA OF THE CLITORIS

Sonya Arina Monen, M.D., Brooklyn, N. Y.

(From the Gynecologic Service of the Kings County Hospital)

PRIMARY carcinoma of the clitoris occurs very infrequently, but involvement of the clitoris in malignancy of the vulva is not unusual. It forms about 16 per cent of vulval cancers. From a study of reported cases, it appears that an average of 11.7 per cent of operative cases are free from recurrence for five years. Taussig's results after radical operation are the most encouraging.

M. G., sixty-three years of age, was admitted to the Kings County Hospital, on Oct. 29, 1932, with the following complaints:

1. Tumor mass protruding from the upper margin of the labia, painful and bleeding, after excessive activity.
2. Pruritus vulvae of long duration.
3. Progressive loss of weight and weakness.
4. Burning, frequent urination.

The previous history is essentially negative, except for pallor and palpitations. She had never borne any children.

For several years, the patient has had pruritus vulvae. In spite of all therapy, this has continued, with periods of exacerbation, and remission. About one year ago, she noticed a small nodule in the region of the clitoris. The family physician stated that the growth was then not malignant, and did not require removal. With an aggravation of the pruritus, and consequent scratching, the mass became swollen and painful. About six months previous to admission, she observed an increase in size, and slight bleeding after excessive walking. Since then there was a gradual loss of weight and weakness.

The patient was moderately obese, appeared chronically ill, pale and dyspneic on exertion. The relevant findings were: Heart sounds of poor muscular quality, normal rate and rhythm. Lungs normal throughout. No palpable masses, or points of tenderness in the abdomen. Inguinal lymph glands not enlarged, soft, discrete and freely movable on the underlying structures.

There was a "strawberry-like" ovoid pedunculated mass, deep red in color, involving the clitoris, about 1½ inches long by ¾ inch wide, attached by a relatively thin pedicle. The lower margin of the pedicle was close to the urethra but did not involve it. Below this, involving almost the entire right labium minus, and the middle one-third of the left, there was a white, thick puckered hyperkeratotic area of leucoplakia. The vestibule was normal. The vaginal mucosa appeared uninvolved,

was senile and atrophic. The cervix was senile, the uterus small and atrophic, being smooth and symmetrical in contour, in second degree retroversion, and freely movable. The fornices were free from any induration or masses. No enlarged pelvic glands were palpable, nor could any masses be felt higher in the pelvis.

In view of the fact that the patient had a poor myocardium, and that her general condition did not safely permit the operation of choice, i.e. dissection of the superficial and deep lymph glands, followed by vulvectomy, it was considered sufficient to perform only a complete vulvectomy. Rather than to have a postoperative mortality, it appeared more rational to risk the treatment of any gland metastasis by deep x-ray therapy. On Nov. 23, 1932, under spinal anesthesia, an extensive complete vulvectomy was performed, removing all the tissues, down to the periosteum. Further exploration of the inguinal regions did not reveal any abnormal lymph glands.

The postoperative reaction was very poor, the temperature remaining elevated to 103°, because of infection of the wound (although drains were inserted at the operation, and there was sufficient drainage). The wound gradually healed, granulating in from below, the general condition of the patient was improved, and she was discharged with emphatic instructions to return for x-ray therapy in one month.

The patient did not return to the hospital until three months later. Examination at this time showed that the site of the operation was completely healed, there being no evidence of any local recurrence. In the left groin, just above Poupart's ligament, there was a metastatic nodule, about ½ inch in diameter, hard, not tender, and fixed to the underlying tissues. No other nodules were felt. Vaginally, the introitus was not stenosed; the urethral meatus appeared normal; no pelvic masses were palpable. X-ray study of the spinal column showed compression of the body of the first lumbar vertebra, suggestive of a metastatic new-growth. Hb 85 per cent, R.B.C. 4,288,000, W.B.C. 7,300, polys 64 per cent, lymph 36 per cent, blood chemistry normal. X-ray of the pelvis Apr. 13, 1933, showed metastasis to the pubic bone.

Between April 16 and May 4, 1933, the patient received a course of ten deep x-ray exposures to the inguinal regions, pelvis, and abdomen. On May 10, she was discharged and instructed to report to the out-patient department every month. Again she failed to return for four months.

On Aug. 21, 1933, she was admitted for the third time. The complaints were, pain in the left groin, radiating down to the thigh, and also in the lower spine, especially during change of posture and walking. There was considerable enlargement and matting together of the glands in the left inguinal region, the masses being firm and nodular. There was an area of fluctuation just above Pouparts ligament. The general condition of the patient was fair.

The pain gradually increased in severity, and it became necessary to incise the fluctuating area to relieve pressure. A small piece of grandulation tissue was excised for diagnosis. The wound was infected, and drained a large amount of foul purulent material. This gradually decreased in amount, and the skin appeared to be healing. The patient was discharged on Oct. 10, 1933, and referred to the out-patient department for further care.

She was readmitted on Nov. 1, 1933, complaining of pain in the left groin and leg, a discharging gaping wound in the left inguinal region, and marked weakness. Blood examination showed: Hb 70 per cent, R.B.C. 3,040,000, W.B.C. 33,200, polys 79 per cent, lymph 21 per cent. Considerable loss of weight, marked pallor and asthenia were present. There were no additional signs or symptoms of metastasis to other organs. In the left groin, there was a discharging large open wound about four inches long by two inches deep. Surrounding this for some distance there was considerable induration. There was a profuse foul smelling,

purulent discharge. The edges of the wound were undermined, and it appeared excavated. On Nov. 11, 1933, there was a considerable hemorrhage from an eroded vessel. On November 24 the bleeding recurred. The wound was packed. Glucose was given intravenously and a transfusion was being arranged. The following morning, she again had a profuse, uncontrollable hemorrhage. In spite of all measures, she died November 25, one year after the original operation.

A NEW ALL METAL UMBILICAL CORD CLAMP*

CHARLES EDWARD ZIEGLER, M.D., A.M., F.A.C.S., PITTSBURGH, PA.

TO DICKINSON belongs the credit of being the first to point the way to the only certain means of preventing umbilical infections, even though his method of accomplishing it has not been adopted, namely, the complete removal of

Fig. 1.

the cord stump. I have long been convinced of it, and over a period of more than fifteen years, I have been experimenting with numerous devices with the hope of duplicating Dickinson's results by nonsurgical measures. I believe that I have now accomplished it with the use of a new all-metal clamp which I have designed for the purpose. My first clamp, which has been quite generally adopted during the past twelve years, has given excellent results and has carried me a long way toward my goal which has been attained with the use of the new clamp.

The mechanism and operation of the new clamp are well illustrated by Fig. 1. The jaws are made of stainless steel, are an inch long and 3/16 inch wide; the spring is made of venadium-alloy steel and is chrome-plated. The peculiar design of the spring was found necessary to prevent fatigue of the metal, by distributing the tension placed upon it, and thereby preserve the resiliency and strength of the spring. The clamp is compact and is small, being less than 1⅝ inch in diameter in either direction.

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*Presented at a Meeting of the Pittsburgh Obstetrical and Gynecological Society, April 13, 1936.

On the compression surfaces of the clamp jaws are three rows of fine, sharp teeth which cut through the amnion, facilitating thereby the escape of moisture from the cord stump under pressure.

The clamp should be applied close to the skin margin. In applying it marked traction should be made on the cord in order to grasp the vessels as far down as possible and to include all of the amnion and jelly of Wharton, both of which end at the skin cuff, as you have seen on the screen in the microscopic section of the umbilicus of a newborn infant.

When the clamp has been applied, the retractor forceps should be removed and the stump cut close to the clamp jaws. A piece of gauze should be placed between

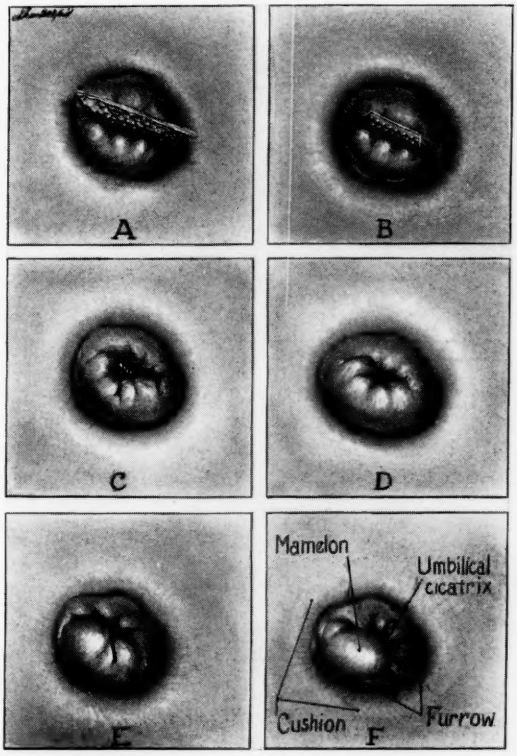

Fig. 2.

the clamp and the abdomen to absorb moisture squeezed from the stump. A binder should not be used. Instead, a piece of gauze bandage should be tied to one arm of the clamp spring, passed around the baby and attached to the opposite arm, to prevent traction upon the stump in handling the baby. Free exposure to the air hastens dehydration of the stump tissues.

In its operation the clamp rapidly produces complete dehydration of all the stump tissues within its grasp. The more powerful the spring, the sooner is the dehydrating process completed. Under the powerful and relentless pressure exerted upon the clamp jaws, the cord stump is compressed into a thin ribbon within a few minutes and in less than eight hours is reduced to a small, translucent, parchment-like film from which every trace of moisture has been removed. The walls of the blood vessels are so thoroughly fused that not a trace of them can be identified

in the film, under a magnifying glass. Secondary hemorrhage is thus impossible with this treatment of the stump and need not be further considered.

The clamp should be removed as soon as dehydration is complete, at any time between eight and twelve hours after birth, and the film trimmed as shown in Fig. 2 (B). Soon thereafter the skin margin of the umbilical ring begins to roll in as the result of the retraction and involution of the umbilical arteries. In forty-eight hours the new umbilicus is already well formed (Fig. 2, C).

All that is left of the cord stump after the film is trimmed is a small, adherent remnant of dried, pressure-necrosed cord tissue which aseptically and hermetically seals both the umbilical vessels and the umbilical ring. This necrosed tissue rapidly crumbles and separates as healing beneath it is completed; in less than a week there is nothing left of it. At no time after the clamp is removed is there an open wound and at no time is there any discharge or even moisture from the umbilicus. There is no visible scar such as follows healing of the granulating wound left when the stump is allowed to slough off. All that can be seen at the bottom of the umbilicus a week after birth are small punctate areas, the sites of the obliterated umbilical vessels.

Little further attention is needed after removal of the clamp. Binder and dressings are omitted. It is only necessary to keep the navel dry until healing is complete.

The drawings of the umbilicus from *A* to *E* (Fig. 2) were reproduced from photographs taken of the same baby at intervals of twelve hours, *A* and *B;* two and one-half days, *C;* four and one-half days, *D;* and *E*, eight and one-half days after birth, respectively. Drawing *F* is "Catteau's Scheme of the Adult Umbilicus" reproduced from Cullen's "The Umbilicus and Its Diseases" (p. 35), original drawing by Broedel.

Compare *F* with *E* taken just before the baby left the hospital.

MEDICAL ARTS BUILDING

Carvalho Azevedo, Fransisco de: The Problem of Voluntary Conception, Ann. Brasileiros de gynec. (Rio de Janeiro) **1**: 255, 386, and 474, 1936.

In an article of 80 pages the author reviews exhaustively the work of Ogino and Knaus and the theory of the "safe period" as a means of contraception. He follows the dictates of Ogino in his recommendations to patients and publishes a convenient table to elucidate the periods of conception in women with all types of menstrual cycles from 21 to 45 days. He reports results of his use of Ogino's method in 50 patients who were personally directed by him over a period of three and a half years; he reproduces graphically the cycles of 19 of the 50 patients which had been followed for more than one year, and adds one other graph of a patient followed 8 months in whom the method failed.

A study of the graphs and a comparison of them with the author's table shows discrepancies between the reckoned periods of conception and the recommended periods of continence in 16, or 80 per cent, of the cases fully reported; the reason for these discrepancies is not clear. Despite this the author reports only two failures: one, the case mentioned above, whose cycles had been charted for only five months previously, and a second, in whom the method was employed after only two periods following an abortion.

To the reader who is interested in the theories of Ogino and Knaus this article offers a scholarly résumé of the literature; whereas to one interested in the clinical reporting of clinical results obtained, the article leaves a decided feeling of uncertainty as to the reliability of the "safe period."

THOMAS R. GOETHALS.

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

A BRIEF EPITOME OF GYNECOLOGIC ENDOCRINOLOGY AND ORGANOTHERAPY

EMIL NOVAK, M.D., BALTIMORE, MD.

THERE is much reason to believe that the general tone of gynecologic organotherapy has been very definitely raised within the past few years as a rather direct result of the gradual permeation of knowledge concerning, at least, the elements of female endocrinology. I have repeatedly urged that the way to teach organotherapy is to teach endocrinology. The salient points of the hormonology of reproduction, if presented to the average medical man in crystallized form, can be absorbed within a few moments. I do not mean that such tabloid teaching is the ideal method, but it will at least convince one that the subject is not quite so hopeless a muddle as some believe, and will enable one to evaluate the endless array of methods and commercial products directed toward the treatment of functional gynecologic disease.

It would probably be safe to assume that most of the readers of this JOURNAL have a working knowledge of the physiology of the female reproductive cycle, but, at the risk of triteness, a few cardinal points may be re-stressed. Just after menstruation a considerable group of follicles begins to mature, though as a rule only one during each cycle is destined to reach full maturation and to ovulate, usually at or near the middle of the intermenstrual period. These growing follicles produce increasing amounts of the follicle hormone, also called by many other names (estrin, estrone, folliculin, female sex hormone, theelin, etc.). This substance is demonstrable in both the blood and the urine by various tests. It occurs in many different forms, of marked degrees of potency, and is found, not only in the follicle, but also in many other body tissues and fluids (placenta, amniotic fluid, urine of pregnancy, etc.).

Moreover, substances of estrogenic type are found in many forms of plants and even minerals, so that this principle cannot be considered a specific hormone of the follicle. Nor does it represent just one substance, but a whole group of substances, and, in the present state of our knowledge, it is better to speak of the estrogenic substances rather than of the estrogenic hormone. This is particularly true since certain chemicals which are not hormones, such as some of the sterol group, are known to be estrogenic also. In spite of recent work purporting to identify one form of estrin as characteristic of the follicle itself, we cannot yet be sure on this point, or on many others concerning the life history of the estrogenic principle.

After the rupture of the follicle and the formation of the corpus luteum, the latter carries on the further production of estrin, so that this principle is present throughout the cycle. As might be expected, however, its amount in the blood drops quite abruptly with retrogression of the corpus luteum, which begins shortly before the onset of the succeeding period.

In addition to estrin, however, the corpus luteum produces a second and more characteristic hormone, progesterone, and this, so far as we know, is produced by no other tissue. It is probably not so sharply distinct from estrin as we formerly believed, for recent studies have shown a very close chemical kinship between the two. It seems not unlikely that progesterone is to be looked upon as only a modified estrin, just as the lutein cell is only a modified granulosal cell.

What are the effects produced by these two hormones? So far as the genital mucous membranes are concerned, and particularly the endometrium, estrin may be looked upon as a growth hormone possessing a remarkably specific effect upon the genital mucosa. It is responsible for the steadily increasing growth and hyperemia which characterize the endometrium from the end of one period to the beginning of the next. Progesterone, on the other hand, brings about the secretory and other changes which characterize the endometrium with the approach of the next menstrual period, changes which are apparently essential for the nidation of the egg if it happens to have been fertilized.

To bring these substances into the picture of chemical organotherapy, estrin is the principle which the clinician utilizes when he administers such commercial products as progynon, progynon B, theelin, or amniotin, in all their various forms. Another estrogenic substance, emmenin, prepared from the placenta by the method of Collip, has apparently been much less extensively used than those just mentioned. Progesterone, on the other hand, is the active principle of such commercial products as proluton, cor-lutin, lipo-lutin, etc.

Important as ovarian hormone function is in the menstrual cycle, it is not as fundamental as is that of the anterior lobe of the hypophysis, which dominates and makes possible ovarian function, as it does that of the thyroid and the adrenal cortex. Two sex hormones are produced by the anterior lobe. One of these, the follicle-ripening principle, is responsible for the maturation of ovarian follicles and thereby the production of estrin. The second, the luteinizing principle, is responsible for the conversion of granulosal and even thecal cells into lutein cells, and thereby the production of progesterone. Evidence is accumulating that these two pituitary sex principles are really separate hormones. It has not been possible to isolate them, although one or two commercial preparations purporting to contain them in at least impure form have been available for experimental clinical use (antuitrin of Parke, Davis & Co., gynantrin of Searle & Co., prephysin of Chappel).

Finally, there is a third pair of sex principles, obtainable from the urine of pregnant women, even in early stages. Indeed, it is upon their presence in the urine that we depend in the Aschheim-Zondek pregnancy test and its various modifications. Together these substances represent the composite called "prolan," consisting of two separate principles which on the ovaries of animals produce either follicle-ripening or luteinizing effects analogous to those produced by the pituitary sex hormones themselves. The evidence now seems quite clear that while these prolan principles of pregnancy urine are very "anterior pituitary-

like" in most respects, they differ in certain important points, and that they are not identical with the pituitary sex hormones themselves. They are therefore commonly spoken of as the anterior pituitary-like gonadotropic principles of pregnancy urine, or as the prolan substances. The follicle-ripening prolan principle is often spoken of as prolan A, the luteinizing, as prolan B. The latter at least is now quite generally considered to be not of pituitary, but of trophoblastic, origin.

It has not been possible to prepare these substances in separate form, but commercial preparations containing both, with apparently a predominance of the luteinizing principle, have been available for some years, and have achieved wide clinical application. The most generally used are antuitrin-S (Parke, Davis & Co.), follutein (Squibb & Co.), and antophysin (Winthrop Co.).

To summarize, therefore, the clinician anxious to practice organotherapy intelligently must know the rôle and significance of the two ovarian hormones, the two pituitary sex hormones, and the two anterior pituitary-like gonadotropic principles (prolan A and prolan B) of pregnancy urine.

Furthermore, he should know enough about the commercial preparations which he employs to be familiar with their hormone content, and he should select preparations made by manufacturers in whom he has confidence.

The other great essential for intelligent organotherapy is to know something of the nature of the endocrine disturbance involved in the functional disorders which he is so frequently called upon to treat, so that he may know what he is trying to accomplish with his treatment. Along many lines our knowledge is still meager and incomplete, but enough has been learned to enable the practitioner to distinguish the rational from the unsound in his attempts at treatment. It would scarcely be possible, within the limits of such a short review as this, to discuss all the endocrine factors which may be involved in the various functional gynecologic disorders which are so frequently encountered by the gynecologist, but it would seem that even a very brief epitome might be of service in differentiating the wheat from the chaff so far as organotherapy is concerned.

In the following discussion, references and citations from the literature are purposely omitted almost entirely, chiefly for the sake of brevity. This paper, in other words, is not a review of the vast literature on the subject, but represents simply what the author considers a sort of minimum working basis for the clinician who would like to treat his cases of functional gynecologic disease intelligently. For a fuller discussion of this and other aspects of endocrinology and organotherapy, as well as for a good working bibliography, the reader will find most useful the recently published volume on *Glandular Physiology and Therapy*, issued under the auspices of the Council on Pharmacy and Chemistry of the American Medical Association.

Amenorrhea.—It need scarcely be emphasized that the primary cause of many cases of amenorrhea, either primary or secondary, is not of endocrine nature, and that organotherapy is therefore not indicated. This applies particularly to such cases as constitutional debility, serious systemic diseases (anemia, tuberculosis, etc.), dietetic deficiencies, etc. When an endocrinopathy is the responsible factor, it most frequently involves (1) the anterior hypophysis and parahypophyseal areas of the midbrain, (2) the thyroid, and (3) the gonads. To say that we can

always differentiate these with precision would be incorrect, and yet it is possible to do so with reasonable certainty in many cases. While blood and urine hormone studies are often of help, the chief reliance must be placed upon careful clinical study, coupled with a familiarity with the characteristic features of each type. For example, the first of the three groups enumerated above is represented by the adipogenital dystrophy (Fröhlich syndrome) cases so commonly observed. In these the amenorrhea and other sex symptoms are due to deficiency of the pituitary sex hormones, while the characteristic obesity is now accepted as due to associated involvement of the hypothalamic and other centers in the vicinity of the anterior lobe.

In the treatment of cases of this type it would be rational to employ preparations of the pituitary sex hormones themselves, but, as stated above, the experience with the few preparations as yet available has not been sufficiently extensive or impressive to justify the statement that they are of much value. The oral administration of pituitary substances of one sort or another is believed by the best authorities to have little or no value, while the employment of the anterior pituitary-like gonadotropic principle of pregnancy urine has likewise proved unsuccessful, since the action of these substances upon the human ovary does not seem at all comparable to their effect upon the ovaries of certain laboratory animals.

Since the gonadal hypofunction in such cases is purely secondary to the pituitary disorder, the use of ovarian hormones is obviously purely substitutional. By giving large amounts of estrogenic substances (theelin, amniotin, or progynon B), for example 10,000 to 20,000 international units daily or every other day for from 6 to 10 doses, bleeding may in some cases occur, usually quite a number of days after the last injection. This, however, is not always the case by any means, and even when it does occur, the bleeding must be interpreted as due to retrogressive changes in an endometrium which has been artificially built up by the endocrine treatment.

Moreover, it must be remembered that such treatment leaves the ovaries untouched, that ovulation is not stimulated, and that, since there is no impetus to the ovarian mechanism, there is no reason to expect a regular recurrence of the bleeding, as in normal menstruation. For such reasons as this, and others which might be mentioned, ovarian therapy has been a disappointment in the treatment of amenorrhea, though, even if the physician is familiar with its limitations, its employment in certain cases is justifiable, as where the psychic effect upon the patient of producing even a spurious form of "menstruation" is an important desideratum. In this connection, the physician can often fulfill a most important function by explaining the innocuousness of amenorrhea in itself, for there is no subject upon which wrong ideas are more prevalent than this.

In the great majority of cases of endocrinopathic amenorrhea, even if there is no obvious manifestation of thyroid deficiency, such as a low metabolic rate, the administration of thyroid substance, usually in the form of the dried extract, is advisable. Just what the mechanism of its effect may be no one seems to know, but it is much more likely to be beneficial than any other form of organotherapy. Where definite thyroid deficiency is evident, the rationale is much more clear, but even without this, a dosage of, in the average case, 1 to 1½ gr. of the dried

extract is not infrequently of much value. In the strikingly hypothyroid cases, the necessary dosage may be considerably larger.

What has been said with reference to the hypopituitary and thyroid cases applies also to the so-called primary hypogonadal cases. In some of these it would seem that the ovaries are really primarily at fault, as where the urine shows an abundance of pituitary sex hormones and an absence of estrin. In many, however, there is much less certainty on this point, and I believe that in not a few of these the ovaries would respond to the pituitary sex stimulation if the latter were forthcoming. The organotherapy of these cases does not differ materially from what has been detailed above, and the results are equally unimpressive.

In all types, the importance of such measures as exercise, general hygiene, and a properly balanced diet, should be impressed upon the patient. In a few cases, where the amenorrhea and the frequently associated obesity or sterility are extremely important problems, and where all other therapy has been unsuccessful, it seems permissible to resort to the tentative and very careful use of light radiation of the hypophysis or ovaries, or both. The procedure is manifestly semi-empiric, especially since there is no selective action of the rays upon any one group of cells. It is certainly not a plan of treatment which should be used frequently or without circumspection, though in our own experience we have noted no harmful results and have had good results in some cases.

Sterility.—Certainly a not inconsiderable group of cases of sterility are explainable on an endocrine basis, but unfortunately we know very little in most instances as to the endocrine factors involved. In some the sterility is associated with amenorrhea, so that the explanation and the treatment are identical with what has been said concerning the latter. Where there is definite evidence of hypothyroidism, thyroid therapy is clearly indicated. This is the most favorable group, so that the clinician is usually rather grateful when he receives a report that the basal metabolic rate is far below normal.

Another type of endocrinopathic sterility is represented by those patients in whom ovulation does not occur, even though menstruation is quite or nearly normal. These "anovulatory" cycles occur most frequently in very young women and those approaching middle life, though they may occur at any age. Their age incidence, in other words, is identical with that of the so-called functional bleeding, which likewise is associated with absence of ovulation and therefore sterility. Can anything be done to correct these? Unfortunately we do not know what endocrine factors are essential for ovulation, though the available evidence indicates that a certain quantitative balance between the two pituitary sex hormones determines the occurrence of the phenomenon. Since this balance differs in different species, and perhaps in different individuals of the same species, the problem of producing ovulation in the human being with our available knowledge and methods seems rather hopeless for the present. To rupture the follicles by bimanual pressure, as has been suggested by some, would not be altogether without hazard, and would probably not be successful, as it is doubtful whether, in the absence of the proper endocrine setting, the ovum would be capable of fertilization or whether follicle rupture would be followed by luteinization and corpus luteum formation. For the present the best plan, admittedly inadequate, seems to be to do everything possible to correct the constitutional and endocrine status of the patient, to give small doses of the inevitable thyroid, and

perhaps to administer the anterior pituitary-like hormones of pregnancy urine during the usual ovulation span, inasmuch as in animals at least these substances are capable of inducing ovulation.

In spite of the uncertainty as to the method of its action, thyroid therapy is quite generally believed to be much more frequently successful in the treatment of endocrine sterility than any other substance. It seems very likely, though there is no proof on this point, that its influence is exerted on the quality of the germ plasm. The doctrine of "defective germ plasm" as a cause either of sterility or habitual abortion is now accepted by the best and the most conservative embryologists, and it seems likely that this is the factor which may be influenced by thyroid treatment. The recent interest in the use of vitamin preparations, such as the germ-oil products, is evidently based on a supposed effect on similar lines, though, as a recent report of the Council of Pharmacy and Chemistry indicates, there is no reliable evidence on this point as yet.

Finally, in the consideration of endocrinopathic sterility, it should be emphasized that a search for endocrine factors in the husband is just as important as in the case of the wife.

Primary Dysmenorrhea.—There is no gynecologic disorder which calls for more thoroughness and individualization in its study than does primary dysmenorrhea. Many factors may enter into its causation, and treatment must therefore vary according to these factors. There is no doubt that some patients are improved by such general measures as exercise, improvement in general hygiene, proper diet, or hematinics when the blood examination indicates their use. It is just as certain that many cases are of psychogenic origin, and that they can be cured by psychotherapy, reassurance, and simple educational talks to the patient. Granting all this, however, there remains a rather large residuum of patients in whom none of these factors are demonstrable, and who seem intractable to any treatment, obtaining palliation only through the use of strong analgesics.

In some of these there is much reason to believe that the underlying cause is of endocrine nature, and that it consists of a qualitative imbalance between estrin and progestine. The studies of Reynolds and others have demonstrated that in general the former is responsible for the normal, rhythmic activity of the uterine musculature, while progestine is the normal inhibitant of this contractility. Incidentally, a similar inhibiting effect is exerted by the luteinizing or prolan B principle of pregnancy urine. It is on this basis that both progesterone and the prolan B principle have attained considerable vogue, following the suggestion originally made by Novak and Reynolds. When used indiscriminately or exclusively, the results are quite sure to be poor. When employed only with due regard to the elimination of other nonendocrine factors, much improvement will be noted in a considerable proportion of cases.

The usual plan for utilizing these preparations is to give daily intramuscular injections of 1 rat unit of progesterone or from 100 to 200 units of one of the pregnancy urine preparations daily, beginning usually three or four days before the menstrual period, and continuing until the flow is well established, when in the typical case the pain itself ceases spontaneously. The two preparations may be alternated or in very severe cases be used in conjunction with each other.

It should be added, and it is indicative of our organotherapeutic floundering in this field, that an exactly opposite plan has been advocated by some, estrogenic principles being used instead of those mentioned above. The biologic basis for this plan seems very unconvincing, and the results even more unimpressive than with the one I have detailed.

Habitual Abortion.—While the corpus luteum is apparently not so indispensable to the continuance of pregnancy in its early human stages, as it is in the case of such animals as the rabbit, there would seem to be no question that it is of considerable importance in these early stages, as it is in the preparation of the endometrium for nidation, In such a distressing condition as habitual abortion, intractable as it so often is to all other measures, it is not surprising, or irrational, that corpus luteum preparations have in the past few years gained wide popularity. Here again thorough study of the patient is necessary to rule out other possible factors, endocrine or anatomic. In most instances it is well to administer small doses of thyroid, even with a normal basal rate.

The use of progesterone preparations may be begun just as soon as the existence of pregnancy is definitely established. In most of the cases of this type reported in the literature, the dosage employed has been very small, much smaller than one would expect to suffice on the basis of physiologic work in animals. This conservatism has no doubt been in part due to the expensiveness of the preparations, though more recently they have become less costly. While the use of ⅕ rabbit unit by intramuscular injection two or three times a week has seemed to be of service in many cases, it would seem that larger doses might be more effective, so that I have usually employed injections of 1 rat unit.

Functional Uterine Bleeding.—This very common menstrual disorder is often a most troublesome one to treat, especially in the case of young patients in whom preservation of the reproductive function is so important. When it affects women approaching middle life, the problem is usually much simpler, for, once the diagnosis is made, radiotherapy can be relied upon in practically all cases for permanent cure. In young women, however, even small doses of radium should be used as infrequently as possible and then with considerable caution, for fear of producing permanent injury of ovarian function.

It is now well established that the ovarian dysfunction concerned in this disorder consists of a failure of ovulation, with abnormal persistence of estrin stimulation and absence of progesterone effect, inasmuch as corpora lutea are not formed. The use of progesterone preparations, therefore, is rational, and has achieved wide popularity. Before progesterone was available for clinical use, the luteinizing principle of pregnancy urine, in the form of antuitrin-S, follutein or similar products, had been utilized for this purpose, with at least a fair measure of success.

When the progesterone preparations are employed, it seems best, when the bleeding is of menorrhagic type, to withhold them until the bleeding has commenced, or even for a few days beyond this, if the bleeding is not too severe. One rat unit may then be injected daily for from 1 to 6 doses, depending on the degree of response. In a considerable proportion the bleeding may be held down to almost normal limits, in others it is only moderately lessened, while in some there will be little or no improvement.

Where the patient suffers from persistent metrorrhagic bleeding, the organotherapy may be begun at once, also with daily injections. The

pregnancy urine preparations still seem to give better results in some instances than progesterone, so that, if the latter fails, 200 rat units of some such preparation as antuitrin-S or follutein may be tried. Or, the two preparations may be either alternated or used in combination.

Uncertain as this treatment is, no more effective organotherapy for this dysfunction is as yet known. In the occasional functional bleedings of definitely hypothyroid origin, thyroid extract is very effective, but these cases are the exceptions. In treating this disorder one is always justified in hoping for an endocrine readjustment to correct the underlying dysfunction, which is located in the pituitary. There is ample justification therefore in doing the best we can with our imperfect organotherapeutic armamentarium, so that the youthful patient may perhaps be tided over her stormy bleeding career until the hoped-for readjustment takes place.

Vasomotor Menopausal Symptoms.—While there is certainly no unanimity on the point, the prevailing viewpoint is that the withdrawal of estrin is the immediate factor in the precipitation of the characteristic vasomotor symptoms of the climacteric. Furthermore there is a rather general acceptance of the view that by far the most frequently effective means of lessening the severity of such symptoms consists in the administration of one or other of the various estrogenic preparations, such as theelin, amniotin, or progynon B. It need not be emphasized that only a minority of women need any organotherapy at all, and that other measures are often of great importance, such as the avoidance of stress and worry, the improvement of general health and hygiene, the use of simple nerve sedatives, etc.

It should be remembered, too, that the symptoms are usually very troublesome only in exacerbations, so that estrin therapy is not continuously indicated. When flushes and sweats come thick and fast, the injection of 1,000 international units, or even less, of the above-named substances every day or every other day, will often be followed by marked amelioration, though usually not complete relief of symptoms. This seems to be true even when cognizance is taken of the psychic effect of the injections. When such improvement occurs, the injections may be stopped, and perhaps small doses kept up by mouth. The oral method of administration is undoubtedly of value, though something like 5 times the hypodermic dose is necessary to produce the same effect. In the milder forms, however, it is likely to be less disagreeable than the hypodermic method, from 1 to 3 tablets or capsules of one of the readily available preparations being used, depending on the mildness or the severity of the symptoms.

Gonorrheal Vulvovaginitis of Children.—The plan of treatment of this troublesome disease which was suggested by Lewis in 1933, appears to have established itself as of genuine value. By building up the epithelial lining of the vagina by means of estrogenic substances, the duration of the infection is very definitely shortened. The vaginal mucosa of the immature child is very susceptible to the proliferative effects of estrogenic substances, so that it can be built up to a close simulation of the postpubertal vagina, which is notoriously resistant to the invasion of the gonococcus. When this method was first suggested, a number of misgivings were expressed as to possible harmful effects. Among these were the effects upon the breasts and the possibility of bringing on uterine bleeding. It is true that swelling of the breasts is occasionally noted, but it is transient, and disappears after cessation

of treatment. Bleeding is practically never evoked, and would likewise not be of serious significance.

The chief objection urged against the plan, however, was that it might, by evoking pelvic hyperemia, predispose to ascent of the gonorrheal infection into the internal genitalia. If one may judge from the literature, however, this objection is theoretical rather than real, so that the method seems to have been accepted as not only justifiable but of real value. Not a great many reports have as yet appeared in the literature, so that its final evaluation still remains for future experience to decide.

The dosage originally recommended by Lewis is 50 rat units hypodermically each day, this corresponding roughly to about 150 international units according to the newer methods of assay. More recently it has been shown that administration by the vaginal route is much more effective than by the hypodermic. This can be done by means of the daily insertion of the vaginal suppositories of estrogenic substances now available.

Senile Vaginitis.—This troublesome condition, occurring not infrequently in women following either a normal or surgical menopause, and associated with vaginal discharge, local irritation, and perhaps pruritus, is caused by infection superimposed upon the atrophic changes occurring after withdrawal of the ovarian secretion. The suggestion has been made (Davis) that the treatment with estrogenic hormone preparations may be effective in throwing off the infection by building up the atrophic mucosa. The results in the small series reported seem to have been favorable, though the treatment may have to be repeated from time to time if the symptoms recur. The dosage recommended is 75 to 100 rat units (about 225 to 500 international units) hypodermically three times a week, the duration of the treatment averaging six weeks.

Other Indications.—Ovarian therapy has been recommended for the condition of painful breasts or "mazoplasia," though its method of action is not clear and the results very uncertain. It is difficult to understand how estrogenic substances can be effective for a condition which many believe to be due to an excessive estrin effect upon the breast gland. Certainly the use of "ovarian residue" by mouth, a method recommended by one writer, has little to commend it, especially as the tablets of ovarian residue are generally accepted as almost or entirely inert.

The puzzling condition of menstrual edema, characterized by striking weight increase and often very obvious edema in association with the menstrual periods, is obviously due to a cyclical disturbance of the water-balance mechanism, though its mechanism is not known. Estrogenic therapy has been tried, and so has the use of the anterior pituitary-like principle of pregnancy urine, but usually without success. In at least one reported case, relief of the symptoms has seemed to follow employment of emmenin (Collip), an estrogenic substance prepared from the placenta and said to be active when given by mouth.

Still other indications might be mentioned, such as menstrual headaches and acne vulgaris, in both of which improvement is said by different observers to have followed the use of estrogenic substances or the pregnancy urine products. So little is known of the hormonal relations of these conditions, and so poorly defined are the results, that there would not seem to be any advantage in discussing them at length.

26 East Preston Street

Department of Maternal Welfare

Conducted by Fred L. Adair, M.D., Chicago, Ill.

MATERNAL MORTALITY STUDY FOR AKRON, OHIO

George A. Palmer, M.D., Akron, Ohio

THIS report is a study in which each hospital maternal death occurring in Akron, Ohio, during the past two years has been individually studied and classified according to the classification adopted by the Hospital Obstetric Society of Ohio. The chief of the obstetric department of the various hospitals is responsible for the presentation of all case histories and pertinent facts of each maternal death occurring in the respective hospitals. Regular quarterly meetings are held by the members of the Society from the various approved hospitals at which time all cases are presented, discussed, classified, and recommendations made whenever necessary, of all deaths occurring in the preceding three months. With all facts at hand, this seems to me to be a most accurate manner of determining the true etiology of all hospital maternal deaths and for any recommendations that will subsequently reduce our maternal mortality.

During the year 1934 there were 4,318 live and stillbirths in the city of Akron. Of this number 1,980 occurred in the hospital. There were 25 maternal deaths which occurred in the hospital. Of the 25 cases only 9 were supposedly normal on entrance to the hospital, and 16 were admitted with known pathology. The 9 patients who died, that were supposedly normal on entrance, include: 2 nonseptic emboli following full-term delivery; 2 septicemia following full-term delivery; 2 hemorrhage: (*a*) postpartum following full-term delivery, and (*b*) following cesarean section for placenta previa; 1 peritonitis following cesarean section; 1 septicemia following cesarean section; 1 shock, full-term delivery, placenta previa.

There were 4 of these 9 deaths which were classified as possible hospital origin: the 2 cases of septicemia following full-term delivery, the case of septicemia following cesarean section, and the case of peritonitis following cesarean section.

The patients admitted to the hospital with known pathology include: 6 septic abortions; 4 ectopics (ruptured); 1 septicemia following home delivery; 2 cardiacs: (*a*) death following cesarean section (noninfectious), and (*b*) late toxemia (noninfectious); 2 toxemias: (*a*) hydatidiform mole (noninfectious), and (*b*) cerebral hemorrhage (noninfectious); 1 pernicious anemia, full-term delivery (noninfectious). Five of the above cases were classified as noninfectious.

During the year 1935 there were 4,164 live and stillbirths in the city. Of this number 2,276 occurred in the hospital. This is a decided increase in the number of hospital deliveries over the year 1934. Also the number of hospital deliveries exceeded the number of home deliveries during the year. There were 25 maternal deaths which occurred in the hospitals. Of the 25 patients only 3 were supposedly normal on entrance to the hospital, leaving 22 which were admitted to the hospital with known pathology. The 3 patients who died that were supposedly normal on entrance include: 2 peritonitis following full-term delivery; 1 shock, full-term delivery, breech, anencephalic monster. The 22 patients admitted to the hospital with known pathology include: 8 septic abortions; 1 ectopic (ruptured); 4 sep-

ticemia following home delivery; 2 peritonitis following home delivery; 2 bronchopneumonia: (*a*) following influenza, home delivery, and (*b*) death before viability; 1 myocardial failure, thyrotoxicosis, seven month's pregnancy (noninfectious); 1

TABLE I

	PREG. AND LABOR NOTHING TO DO WITH DEATH	PREG. AND LABOR NOT PRIMARY	PREG. AND LABOR PLUS CONTRIBUTORY	DEATHS BEFORE VIABILITY	NONINFECTIOUS	EXTRA HOSPITAL ORIGIN	POSSIBLE HOSPITAL ORIGIN	KNOWN PATHOLOGY ON ENTRANCE	SUPPOSEDLY NORMAL ON ENTRANCE	HOME DELIVERY HOSPITAL DEATH	NONRESIDENT	POSTMORTEM
1934	0	1	1	10	10	1	4	16	9	1	1	8
1935	1	4	2	10	7	8	2	22	3	8	2	2
Total	1	5	3	20	17	9	6	38	12	9	3	10

TABLE II

	ABORTIONS	ECTOPICS	LATE TOXEMIA	CARDIAC	HEMORRHAGE	SHOCK	NONSEPTIC EMBOLUS	ANTEPARTUM PNEUMONIA	POSTPARTUM INFECTION	OTHER CAUSES	TOTAL DEATHS
1934	6	4	1	2	2	1	2	0	5	2	25
1935	8	1	2	0	1	1	0	2	8	2	25
Total	14	5	3	2	3	2	2	2	13	4	50
Per cent	28	10	6	4	6	4	4	4	26	8	

TABLE III

HOSPITAL		LIVEBIRTHS	STILLBIRTHS	TOTAL BIRTHS	MATERNAL DEATHS	SUPPOSEDLY NORMAL ON ENTRANCE	PER CENT NORMAL	KNOWN PATHOLOGY ON ENTRANCE	PER CENT PATHOLOGY	HOME DELIVERY HOSPITAL DEATH	DEATH RATE TOTAL BIRTHS	DEATH RATE VIABLE BIRTHS	DEATH RATE POTENTIALLY VIABLE BIRTHS	ABORTIONS	PER CENT ABORTIONS
A	1934	958	37	995	13	3	23	10	77	1				3	
A	1935	1,118	32	1,150	12	1	8	11	92	3				5	
A	Total	2,076	69	2,145	25	4	16	21	84	4	1.16	1.20	0.62	8	32
B	1934	436	10	446	6	3	50	3	50	0				2	
B	1935	570	15	585	5	0	0	5	100	2				2	
B	Total	1,006	25	1,031	11	3	28	8	72	2	1.06	1.09	0.49	4	36
C	1934	526	13	534	6	3	50	3	50	0				1	
C	1935	515	26	541	8	2	25	6	75	3				1	
C	Total	1,041	39	1,080	14	5	35	9	65	3	1.29	1.34	0.86	2	21
Grand total		4,123	133	4,256	50	12	24	38	76	9	1.17	1.21	0.65	14	28

eclampsia following home delivery (noninfectious); 1 acute hemorrhagic nephritis (noninfectious); 1 nephritic toxemia, full term (noninfectious); 1 premature separation of placenta, cesarean section, seven months' second-degree burns of back and thighs (noninfectious). Five of the above cases were classified as noninfectious.

The above data for both the years 1934 and 1935 are classified in Tables I and II. There are additional headings on the classifications adopted by the Society, but inasmuch as there were no cases in this particular study of those types, the additional headings were omitted.

DISCUSSION

Of the total number of deaths for the two-year period, 38, or 76 per cent, had known pathology on entrance to the hospital. Only 12 cases, or 18 per cent, were supposedly normal on entrance to the hospital. Just 6 cases, or 12 per cent, were classified as possible hospital origin. This rather speaks for the safety of hospital as compared with home delivery. This report definitely indicates that the hospitals have been unjustly credited with maternal deaths that rightfully do not belong to them. I feel that comparable studies made throughout the country will show a similar condition to exist. The death rate, based on all births, is 1.17 per cent, while the rate based on only the potentially viable births is 0.65 per cent. The figures on abortion as a cause of death are quite astounding. When we consider that 14 or 28 per cent of the total number of deaths are due to abortion, we should be cognizant of the fact that it is time for the medical profession to swing into action to remedy this situation. The patients who died as a result of shock, hemorrhage, and postpartum infection are the type of case in which we have great hopes that this Society and similar organizations will be effective in reducing this mortality to a decidedly lower figure.

SUMMARY

1. Seventy-six per cent of all patients dying in the hospital were admitted to the hospital with known pathology on entrance.

2. Only 12 per cent of the total deaths can be attributed to possible hospital origin.

3. Deaths as a result of abortion accounted for 28 per cent of the total number of deaths.

4. Nine of the deaths attributed to the hospital were patients who were delivered in the home and subsequently sent into the hospital.

5. The death rate based on potentially viable births is 0.65 per 1000.

6. Similar accurate analytical and statistical studies should be made in other localities to determine the true etiologic factors responsible for our high maternal mortality.

7. Patients dying as a result of hemorrhage, shock, postpartum infection, and abortion as described in this report, are the type of cases which the medical profession can, by proper control, eliminate for the most part, thus reducing our all too high maternal mortality in this country.

623 First Central Tower

American Journal of Obstetrics and Gynecology

EDITORS: GEORGE W. KOSMAK, M.D., AND HUGO EHRENFEST, M.D.
ASSOCIATE EDITORS: HOWARD C. TAYLOR, JR., M.D., AND WILLIAM J. DIECKMANN, M.D.

Editorial Comment

THE relief of pain in childbirth ever has been the objective of obstetricians but practical success has only been attained in more recent times. Many anesthetics and hypnotics have been tried and recommended for the production of analgesia and amnesia in labor. It is clear that every drug producing these effects must not only alleviate the mother's discomfort but must not jeopardize the safety of the child. Every analgesic used in labor should, therefore, be scrupulously studied as to its effects on both the maternal and fetal organism. This applies in particular to barbituric acid derivatives, for these substances have in the past few years gained preeminence as obstetric analgesics.

The data concerning the action of barbiturates on the several functions and organs of the body are abundant, while the effect of these drugs on the fetus has not been studied adequately. It was only quite recently that information on this subject became available, partly clinical and partly experimental in nature.

Fabre administered to one pregnant dog a daily dose of 0.5 gm. of barbital by mouth for five days before delivery, and reported the discovery of diethylbarbituric acid in the fetus. Boucek and Renton, on the other hand, gave amytal to pregnant rats near term and tested the viability of the fetuses by mechanical stimulation. They observed that there was no depression of the fetuses when amytal was administered to the mother, and hence concluded that the placenta is not permeable to amytal. We have, then, two conflicting reports on the permeability of the placenta to barbiturates.

More recently Koppanyi's methods on the extraction and quantitative determination of barbiturates made it possible to study this subject in an exact and quantitative manner. Working in Koppanyi's laboratory and using his methods Dille found that the placenta presented no barrier to the passage of either barbital or amytal. The fetus in taking up the barbiturate from the blood of the adult body behaves like an organ of the adult body, the barbiturate reaching a

maximum concentration rapidly in the fetus with a fall in the concentration of the barbiturate in the maternal blood. The concentration of the barbiturate may reach a fairly high level in the fetus. In some cases this concentration approaches and reaches anesthetic levels.

Dille's earlier results were obtained with the injection of *full anesthetic* doses of barbiturates, and the objection was raised that in the obstetric practice such doses were not employed. To meet this objection he performed a series of experiments using only hypnotic doses of barbital in pregnant rabbits near delivery, and found not only that barbital is transmitted through the placenta even in *hypnotic* doses, but also that the concentrations of barbital in the fetus are directly proportional to the size of the dose administered to the mother.

The clinical studies on the effect of barbiturates on the offspring did not yield uniform or conclusive results. To quote only a few investigations: Morehead and Mussey reported no ill effects on the offspring with small doses of amytal given to the mother by mouth. With larger doses Swendson observed that about one-third of the babies were somewhat apneic at birth, and Shir and Daichman reported that following the use of barbiturates in labor the babies were frequently narcotized.

The conflicting clinical results are obviously due to the size of the dose of barbiturates used during labor. It is not to be expected that the fetus will show lesser effects from the drug than the mother. Dilie's investigations have proved beyond any doubt that the barbiturates permeate the placenta, and the concentration of barbiturates in the fetus depends upon the size of the dose given to the mother. Entirely aside from the dangers to the mother which may result in administering a fixed anesthetic, the barbiturates present definite hazards to the child and to the course of labor. It is very important and essential therefore that greater care be exercised in their administration. In addition, the frequently observed prolongation of labor associated with the employment of analgesic preparations must have an important bearing on stillbirth and maternal mortality rates.

Kraus, E. J.: The Pathogenesis of Galactorrhea, Arch. f. Gynäk. **155**: 380, 1935.

The proliferation and hypertrophy of the milk ducts during pregnancy is the result of stimulation by the ovarian hormones. The lactation hormone is probably a product of the pregnancy cells which cannot be activated until the placental influence has been removed.

The author describes two instances of galactorrhea in nulliparas both of whom showed some degree of hyperpituitarism. Both had hyperplasia of the eosinophiles of the anterior lobe with proliferation of the hypertrophic main cells. In both, the ovaries were degenerated. These changes in the pituitary were due to pressure, one following a tumor of the third ventricle and the other a tumor of the sella turcica.

RALPH A. REIS.

Correspondence

August 19, 1936.

To the Editor:

There are several statements in Dr. Kanter's article (Am. J. Obst. & Gynec. **32**: 183, August, 1936) on fibroids in which reference is made to my publications on the same subject. Perhaps further discussion of these statements will tend to establish our respective positions and will clarify the subject matter for the reader in general.

In *Surgery, Gynecology and Obstetrics* (**61**:743-750, 1935), I made the statement, "The hypothesis that all forms of overgrowth of the uterine endometrium or musculature are due to the same factor, the estrogenic principle, is not only supported by clinical and pathologic data, but also explains satisfactorily the simultaneous development of endometrial hyperplasia, endometriomas and uterine fibroids, with their associated clinical features, hemorrhage and sterility." From a study of 100 cases of uterine fibroids, Dr. Kanter undertakes to evaluate this theory.

Dr. Kanter brings up the point, and a very true one indeed, of the infrequency of endometriosis in the colored woman with fibroids. He states: "Witherspoon further deduces that the same etiologic factors (the estrogenic principle) are active in producing adenomyosis, a condition that was relatively rare in our colored patients but *common in the white woman who had no evidences of pelvic inflammatory disease* [italics mine]. This becomes increasingly difficult to understand since the colored woman had, as a rule, larger tumors, a fact that would suggest a greater excess in the circulating estrin content." The infrequency of endometriosis in colored women with fibroids is a well-known clinical fact, but there is, to me, a rational explanation for the rarity of its occurrence in this race, namely, the high incidence of salpingitis, with resulting occluded tubes. Retrograde menstruation with peritoneal, ovarian, etc., inoculations with uterine endometrium cannot occur through a blocked tube; hence the infrequency of endometriosis in the colored woman. Conversely, the high incidence of endometriosis in the white woman with fibroids (64 per cent in my series) can be explained on the same basis, the relative lack of salpingitis in the Caucasian, with resulting opportunity for retrograde menstrual endometrial implants to occur through patent tubes. Of course, complete belief in metaplasia-of-serosal-cells origin of endometriosis discredits this explanation.

Another point which Dr. Kanter mentions is, "If hyperplasia of the endometrium can be taken as a criterion of excessive estrin stimulation, one would expect to find more than a 53 per cent (his figure) incidence in a series of patients with fibroids." Cannot this apparent discrepancy with the original hypothesis be explained by the well-known fluctuating levels of estrin? Granted that the estrin stimulation was at one time sufficient to produce endometrial hyperplasia and fibroids, it does not necessarily follow that this level has to be maintained continually. Once the fibroids have been formed, their change to estrin fluctuations is minimal, while endometrial changes to the estrogenic hormonal level is much more sensitive and rapid. Possibly Dr. Kanter operated upon his patients at a time when half of them were at a low estrin phase.

And a last point which Dr. Kanter makes is, "Again, we must disagree with Witherspoon's contention that the sterility associated with fibromyomas is explained

totally by the hyperestrinism he believes is produced by the atretic follicles in the absence of corpora lutea.'' I firmly believe that on this point there must be a misinterpretation of my explanation for the associated sterility; my statement reads, ''The explanation for the sterility in these three conditions (endometrial hyperplasia, fibroids, and endometriosis) is undoubtedly *lack of ovulation*, so well demonstrated in the ovaries by the presence of multiple follicle cysts and the absence of corpora lutea.'' I meant merely to infer by this statement that lack of ovulation (not hyperestrinism) was the cause of the associated sterility in women with fibroids, granted that mechanical factors (salpingitis, etc.) were excluded.

There are two experimental observations by Lacassagne relative to this subject that are of value: (1) ''Progressive change in the uterus of rabbits submitted from birth to repeated injections of estrone'' (Compt. rend. Soc. de biol. **120**: 685-689, 1935), ''Beginning on the third day of their birth six female rabbits were given weekly injections of folliculin benzoate, the amount being gradually increased from 1,000 international units to a maximum dose of 10,000 units after the lapse of two months. Five of the animals were sacrificed after 73, 99, 130, 169, and 851 days, respectively. It was found that the treatment had elicited a *fibromyomatous* transformation in the uterine wall and adenomatous proliferation in the cervix and the tubes. The findings strengthen notably the position of those clinicians who have long been referring endometrial hyperplasia, as well as uterine fibroids, to an excessive secretion of hormones.'' (2) ''Progressive changes in the mouse uterus under the prolonged administration of estrome'' (Idem **120**: 1156-1158, 1935). ''Weekly injections of 300 international units of estrone benzoate produced in the mouse uterus, after 11 to 584 days, changes resembling those already described in the rabbit.''

J. Thornwell Witherspoon, M.A. (Oxon), M.D.
4008 N. Pennsylvania Street, Indianapolis, Ind.

REPLY BY DR. KANTER

Answering Dr. Witherspoon's letter of August 19, I have had the privilege of reading his letter previous to submission for publication. At that time I made the following comments to Dr. Witherspoon while urging him to publish his communication in order to stimulate interest in the subject.

We agree that the lack of endometriosis in colored women may be explained on the basis of the frequency of occurrence of salpingitis with closed tubes, but it fails of comprehension in explaining the similar rarity of internal endometriosis (adenomyosis) in this class of patient, this latter condition having no obvious relationship to closed fallopian tubes.

With regard to Dr. Witherspoon's explanation of the varying endometrial pictures found by us in our study, suffice it to say that such a question cannot be settled satisfactorily until such a time as a correlated study of blood estrin levels and endometrial histology is made upon a large series of patients.

Finally, Witherspoon contends lack of ovulation is the responsible factor in the production of sterility in patients with the fibroid, endometrial hyperplasia, endometriosis complex. The fact that we found corpora lutea in various stages of degeneration proves conclusively that these patients do ovulate.

Again, I feel that Dr. Witherspoon has done a great service in the field of research study. Such controversies are healthy and should serve to stimulate others to study these problems and possibly help us to settle the points that are in question.

Aaron E. Kanter,
310 S. Michigan Ave., Chicago, Ill.

To the Editor:

In the August number of the JOURNAL in an article on "Triple Pregnancy Diagnosed by Means of X-ray," Margaret B. Ballard says, that a careful search of the available literature reveals only nine cases in which a diagnosis of triplets was made before delivery (Edling, Essen-Moeller, Favreau and Despons, Gennell, Johnston, Marcus, Rowden, Trillat, Eparvier and Naussac and Aldredge). She then briefly describes these nine cases and adds a case of her own. In Edling's case the correct diagnosis was made only after delivery.

For the sake of completeness, may I add two more cases. In 1923 I presented an illustration of the third case reported in the literature of triplets demonstrated on an x-ray plate. (The Value of X-ray in Obstetrics, *Medical Clinics of North America* 7: 611, 1934.) The two reports which preceded this article were those by Edling and by Essen-Moeller. My case was similar to that reported by Edling in one respect, namely, that the correct diagnosis was not made until the x-ray plates were reexamined after delivery. In Edling's case an x-ray picture taken at the fourth month resulted in a diagnosis of twins, but after delivery, evidences of the third baby were discovered on the x-ray plate. In the case I reported, a diagnosis of triplets or twins with polyhydramnios was made before delivery. An x-ray picture was taken but only two heads were seen. However, after delivery of the three babies, reexamination of the x-ray plate revealed the third head.

The second case I should like to add is that reported by Weil (Grossesse Trigémellaire, *Gynécologie et Obstétrique* **32**: 289, 1935). In two additional cases of triplets reported by Weil the x-ray plates aroused a suspicion of triplets but three fetuses could not be definitely detected on the x-ray plates.

In the world literature there are four cases of quadruplets demonstrated by x-ray examination. The first was reported by Hermstein and Pfalz (München. med. Wchnschr. **78**: 492, 1931). The second and third cases were reported by E. U. Williams (Brit. M. J. **2**: 1206, 1935). The fourth case was reported by Dawson (J. Obst. & Gynaec. Brit. Emp. **43**: 252, 1936).

J. P. GREENHILL, M.D.,
55 E. WASHINGTON STREET,
Chicago, Ill.

Umbilical Cord Clamp

To the Editor:

In my article describing an improved umbilical cord clamp, published in the September, 1936, issue of the JOURNAL, page 513, I failed to give credit to Dr. Charles E. Ziegler of Pittsburgh, Pa., who described a special device of this kind in a paper entitled "Additions to Our Obstetric Armamentarium," which appeared in the JOURNAL in January, 1922.

The latter was published two months prior to the paper by Willson, referred to by me and which was included in the March, 1922, issue of the same JOURNAL.

MILTON E. KAHN, M.D.
BUFFALO, N. Y.

Department of Reviews and Abstracts

Conducted by Hugo Ehrenfest, M.D.

Selected Abstracts

Physiology of Labor

Robinson, Datnow, and Jeffcoate: Induction of Abortion and Labour by Means of Oestrin, Brit. M. J. **1**: 749, 1935.

It is believed that during pregnancy expulsive contractions of the uterus are held in abeyance by a state of equilibrium in the hormones, progestin and estrin. These hormones have been shown to have a contrary effect on the uterus, the former inhibiting, the latter stimulating, uterine activity. Induction of labor with estrin was accomplished in rodents but not in human beings.

Estrin is not directly oxytocic; it has no effect on the isolated uterus and only acts when given parenterally to the animal. It has a long latent period of activity, and produces its effect (1) by causing hypertrophy of the muscle fibers and hyperemia of the uterus, (2) by sensitizing the muscle and nerve elements of the uterus, and (3) by stimulating the production of infundibulin in the body.

A series of experiments in the human being is recorded, showing results obtained with the use of estrin during different stages of normal and abnormal pregnancy. The hormone was effective in stimulating uterine activity in cases of missed abortion, thus confirming the work of others who claim that the retention of the dead fetus is associated with an absence of estrin in the blood. Estrin is useful in primary uterine inertia.

F. L. Adair and S. A. Pearl.

Knaus, H.: The Causes of the Onset of Labor. Med. Klin. 30: 1649, 1934.

In the opinion of Knaus the onset of labor is dependent upon two factors. The first is the uterine musculature. During pregnancy, the uterine muscle gradually increases its tonicity and power of contractility. When the corpus luteum degenerates, it releases its control on the uterine musculature so that the muscle may react to the hormone of the posterior pituitary lobe. This hormone is what initiates labor. As long as the corpus luteum is active the posterior pituitary secretion cannot act on the uterine muscle. This pituitary secretion is also influenced by the placenta, because it contains a substance (the anterior pituitary-like hormone) which has a luteinizing effect. Whereas the estrus hormone produced by the placenta increases with the duration of pregnancy, the pituitary-like hormone production in the placenta decreases with the advance in pregnancy. The result of this is that the corpus luteum gradually degenerates in the second half of pregnancy. As this occurs the highly contractile uterine musculature becomes more and more susceptible to the posterior pituitary secretion. At the end of pregnancy, the corpus luteum has absolutely no inhibitory effect on the uterine muscle, and the posterior pituitary hormone acts on the uterine musculature to initiate labor.

J. P. Greenhill.

Voron and Contamin: Induction of Labor by the Combined Use of Folliculin and Pituitary Substance in Prolonged Pregnancy, Bull. Soc. d'obst. et de gynéc. **24:** 68, 1935.

Because it is known that folliculin sensitizes the uterine musculature to the action of an oxytocic, the authors attempted to use both folliculin and posterior pituitary substance in three cases of prolonged pregnancy. In two cases they obtained contractions within a few hours after the injections were given. The contractions continued until the fetuses were expelled. The authors, therefore, recommend this procedure and consider it entirely harmless.

J. P. GREENHILL.

Bock, A.: pH Determinations of the Vaginal Secretions and of the Amniotic Fluid in an Attempt to Determine Rupture of the Membranes, Arch. f. Gynäk. **155:** 443, 1934.

The author made pH determinations of the vaginal secretions and of the amniotic fluid of pregnant women in the attempt to discover a possible change after rupture of the membranes.

He found that the pH concentration of the vaginal secretion was 5.2 to 6.0 when the membranes were still intact. He ascertained values of 7.0 to 7.5 for the amniotic fluid. The values in the vaginal secretions in healthy women in labor and after the rupture of the membranes were 7.0 or higher. He, therefore, concludes that pH concentration of 6.0 or less is definite evidence that the membranes are intact.

RALPH A. REIS.

Coatz, Alberto S.: The Etiology of Premature Rupture of Membranes, Obst. y ginec. (Buenos Aires) **14:** 529, 1935.

The author found the incidence of premature rupture of the membranes to be 8.3 per cent. In 81 per cent of cases the rupture of the membranes occurred at the end of labor. There is no relationship between the time of rupture of membranes and the constitution of the patient or the growth of the pregnancy. Of the cases studied, 60 per cent were multiparas.

Occupation, coitus, traumatism have no influence on premature rupture of membranes. Metritis and its consequences, abnormal adhesions and great thinness of the membranes could be causative agents.

The author believes that neither malposition of the presenting part nor false labor pains lead to premature rupture of membranes.

MARIO A. CASTALLO.

Winter, E. W.: The Premature and Very Early Rupture of the Membranes, Monatschr. f. Geburtsh. u. Gynäk. **99:** 332, 1935.

At the Giessen Clinic among 573 women who had premature rupture of the membranes, 4 women died as the result of this complication. Likewise, 9 per cent of the viable children also perished as the result of the untimely rupture of the membranes. Hence, the author considers this complication to be a very serious one. It occurs in about 20 per cent of all cases. Many women developed puerperal infections. Intrauterine manipulation must be carried out more frequently and serious consequences may result from this. The longer the period of time which intervenes between rupture of the membranes and the onset of pains the worse the prognosis. Every woman who has premature rupture of the membranes should be delivered in a hospital.

J. P. GREENHILL.

Higgins, L. G.: Induction of Labour, Brit. M. J. 2: 721, 1935.

The author presents clinical data indicating favorable results from simple rupture of the bag of waters for induction of labor. These views are supported by observations made by Fitzgibbon, Morton, Berger and Stroganoff on normal, postmature, and eclamptic patients, respectively.

The author believes this method of induction approximates closely to the normal onset of labor. It is suggested that there is no evidence that artificial rupture of the membranes under suitable conditions increases the tendency to pyrexia in the puerperium. Nor has any relation been established between pyrexia and the length of time which elapses between artificial rupture of membranes and the onset of labor. No prejudicial effect upon the child due to early rupture of the membranes has ever been ascertained.

F. L. Adair and S. A. Pearl.

Blair, E. Murray: Induction of Labour by Rupture of the Membranes, Canad. M. A. J. 34: 49, 1936.

The author discusses inductions of labor in general and points out the failures with medical routines. He outlines the actions of the various factors before labor can be precipitated as: (1) The presence of estrin in sufficient quantity to (a) sensitize the uterine fibers and (b) call forth enough infundibulin to cause contractions; (2) the absence of progestin, enough that the contractions be not inhibited; (3) enough infundibulin must be brought into the circulation by estrin to promote labor contractions.

It is pointed out that rupture of the membrane is a means of inducing labor; that "dry labor" is not the bugbear it was once considered; and that rupturing the membranes has a place in the treatment of eclampsia.

He concludes that rupture of membranes is the surest procedure in inducing labor at full term; its risks are not as great as they have been considered. However, he does not uphold rupture of the membranes as a routine method of induction.

H. Close Hesseltine.

Furtado, Affonso Henriques: Fetal Asphyxia Due to Artificial Rupture of the Membrane in a Case With Membranous Insertion of the Cord, Rev. de gynec. e d'obst. 29: 629, 1935.

This report concerns a multipara, aged thirty-seven, who had been in labor for four hours. She was progressing normally, the fetus in cephalic position, the fetal heartbeats 140 per minute. After complete dilatation of the cervix, the membranes were ruptured artificially. Ten minutes later the patient delivered an apparently dead baby which was, however, revived by artificial respiration. The placenta was delivered spontaneously forty minutes after the baby was born. On examination of the placenta it was found that the cord was attached to the membranes.

F. L. Adair and J. Suarez.

Ganner, Philip J.: Results of Ante-Natal Administration of Quinine, Brit. M. J. 2: 205, 1935.

The use of quinine in the last weeks of pregnancy is revived. The idea is an old one, but the literature on the subject is scanty. Certain advantages are claimed for it by those who used it, and, therefore, it deserves further trial.

The author reports a series of 50 normal primiparas who received 2 gr. of quinine bihydrochloride t.i.d., from the thirty-sixth week of pregnancy onward. The results

are tabulated, and he concludes that the tendency to onset of premature labor is diminished by the antenatal administration of quinine and that the first and second stages of labor are accelerated without damage to mother or child. Inertia is not entirely abolished. In his small series of cases, there were no retained placentas or severe postpartum hemorrhages. An increase of uterine activity possibly exists in the third stage also. There appears to be no evidence of any influence on involution and the puerperium.

In all, the uterine action is strengthened by giving small doses of quinine during the last month of pregnancy. Since good uterine contractions are a very valuable factor in obstetrics, this method becomes commendable, if the fact is finally established and accepted by the profession. A method which secures good uterine contractions and is simple and safe for use in domestic practice deserves thorough investigation and more attention than it has had up to the present time.

F. L. Adair and S. A. Pearl.

Mitchell, D. A., and Bradbrooke, H. N.: Further Experience of the Use of Quinine in Normal Labor, Brit. M. J. 2: 206, 1935.

In 1930, the author had published material on the use of quinine antepartum in a series of 400 cases. He adds enthusiastically to its merits in the present study. Claim is made that the general health of the patients is improved due to the tonic action of quinine in small doses. Often dyspepsia and heartburn in the later weeks of pregnancy are corrected by it. Labor is made easier and shorter. The first stage of labor proceeds almost imperceptibly and painlessly to the patient. The second stage is more forceful and shortened. Uterine retraction is uniformly good. Clots were rarely seen forty-eight hours following labor in the series of quininized patients. There is no increased tendency to premature or precipitate labor. Retained placenta is uncommon; in fact, cases with a history of such and postpartum hemorrhage in previous labor were treated successfully with quinine prenatally. Perineal lacerations and afterpains are not increased by its use. In the abnormal cases each one must be considered on its own merits. The drug is of greatest aid in normal labor; it is contraindicated in any condition in which slow labor is desirable for the purpose of molding.

The author emphasizes the administration of the drug in small repeated doses. Attempts to use larger doses will only bring the method into disrepute. Quinine has not been proved to be an initiator of uterine contractions. It acts as a tonic, increasing the basic tone of the uterine muscles, and reinforces contractions which are excited by endogenous means. This tonic action is produced by a small dose; larger doses may cause inertia or paralysis of uterine muscles. The dose should not exceed 1½ to 2 gr. t.i.d. for two to three weeks before labor is expected. A single daily large dose is contraindicated.

F. L. Adair and S. A. Pearl.

Goecke, H.: The Significance of the Number of Pains in Cases of Premature Rupture of the Membranes Especially in Primiparas With Normal Pelves, Monatschr. f. Geburtsh. u. Gynäk. **99:** 24, 1935.

During the past few years Frey has written many articles attempting to prove that a knowledge of the actual number of labor pains is of the utmost significance in the conduct of labor. Frey claims that if labor does not terminate spontaneously after a specific number of labor pains, depending upon the parity and intactness of the membranes, interference will become necessary. Goecke studied a large series of cases but could not substantiate Frey's contention. He found that patients did deliver spontaneously after they had passed the so-called maximum number of

uterine contractions. He therefore warns against terminating labor by artificial means simply because a patient has had a certain number of labor pains. This warning is particularly important in cases where Frey's maximum number of pains is exceeded before there is complete dilatation of the cervix and where therefore a cesarean section or other operation would be advocated by him.

J. P. GREENHILL.

Defendi, S.: The Number of Uterine Contractions During the Various Phases of Labor, Folia Gynaec.-demog. **32**: 529, 1935.

The author states that the results obtained from the counting of the uterine contractions during the labor of 110 primiparas and 100 multiparas, done according to the theory of Frey, demonstrate such a variability of values that these do not permit acceptable deductions in regard to prognosis or necessary interference.

MARIO A. CASTALLO.

Consoli, D.: The Action of the Lower Uterine Segment During Labor, Clin. Ostet. **37**: 385, 1935.

After briefly describing the anatomy and histology of the uterus, the author discusses the action of the lower uterine segment during labor. He concludes that during labor two phases can be distinguished in the lower uterine segment:

1. A passive one designated by the contractions of the two internal layers of the uterus with a minimal participation of the external longitudinal layer, which only serves at this period to support and coordinate with the functions of the other layers. The lower uterine segment at this time is simply stretched, having no sign of contractions in its fibers. Such passive distention, due to the descent of the ovum, reduces the tonicity of the fibers of the uterine os and produces dilatation.

2. The other phase is active and is designated by the contractions of the external layer. The transmission of the contractions of the longitudinal fibers of the body to the lower segment causes a shortening of the cervical margins, giving rise to the real progress of dilatation, which finally leads to the termination of labor.

AUGUST F. DARO.

Sciclounoff, T.: Inquiry Into the Value of Rectal Examinations During Labor, Rev. franç. de gynéc. et d'obstet. **30**: 1, 1935.

The author sent out 280 questionnaires concerning the value of rectal examinations. He received 115 answers, and from an analysis of these replies he comes to the following conclusions: Rectal examinations alone are used by only 7.9 per cent of obstetricians. It is considered by 72 per cent to be insufficient for all normal and abnormal cases. However, 21 per cent of obstetricians believe that rectal examinations suffice for normal cases but not for the abnormal ones. The majority of obstetricians believe that vaginal examinations are indispensable for midwives. The majority of heads of departments permit vaginal examinations to be made by students. Three-fourths of all the obstetricians who answered consider vaginal examinations harmless when practiced according to a rigid technic. The author himself maintains that labor may be conducted in the large majority of cases by external examinations alone. When necessary, vaginal examinations should supplement abdominal examinations. He is opposed to rectal examinations because they are much more difficult to make than vaginal examinations, and it is difficult to teach students by this method.

J. P. GREENHILL.

Farkas, J.: The Question of the Movable Head in Primiparas, Monatschr. f. Geburtsh. u. Gynäk. **100:** 138, 1935.

In the Budapest Midwife School, Farkas found that among 3,829 primiparas, the head was floating at the inlet in 305 cases, an incidence of 8 per cent. The pelvis was contracted in only 50 of these women, hence the head was movable in 6.7 per cent of all primiparas with normal pelves. In 87.3 per cent of these women, delivery occurred spontaneously; therefore a movable head in a primipara is not necessarily a pathologic condition. In fact, in 15 per cent of the cases, labor was completed within a very short time. In the author's opinion the chief cause for the delay in the engagement of the head lies in the increased resistance of the lower uterine segment and not in the condition of the abdominal wall or the uterine contractions. The author advises that primiparas in whom the head is not engaged at the onset of labor should be delivered in a hospital.

J. P. GREENHILL.

Items

American Board of Obstetrics and Gynecology

The next written examination and review of case histories of Group B applicants by the American Board of Obstetrics and Gynecology will be held in various cities in the United States and Canada on Saturday, March 6, 1937.

The next general examination for all candidates (Groups A and B) will be held in Atlantic City, N. J., on June 8 and 9, 1937, immediately prior to the American Medical Association meeting.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania. Applications for these examinations must be filed in the Secretary's office not later than sixty days prior to the scheduled date of examination.

The American Board of Internal Medicine (Inc.)

The American Board of Internal Medicine, incorporated February 28, 1936, completed its organization on June 15, 1936. The officers chosen were Walter L. Bierring, M.D., Des Moines, Chairman; Jonathan C. Meakins, M.D., Montreal, Vice-Chairman; and O. H. Perry Pepper, M.D., Philadelphia, Secretary-Treasurer. These officers with the following six members constitute the present membership of the Board: David P. Barr, M.D., St. Louis; Reginald Fitz, M.D., Boston; Ernest E. Irons, M.D., Chicago; William S. Middleton, M.D., Madison; John H. Musser, M.D.; New Orleans, and G. Gill Richards, M.D., Salt Lake City.

The term of office of each member will be three years, and no member can serve more than two consecutive three-year terms.

The organization of the Board is the result of effective effort on the part of the American College of Physicians in conjunction with the Section on Practice of Medicine of the American Medical Association and these two organizations are represented in the membership of the Board on a five to four ratio, respectively.

The American Board of Internal Medicine had previously received the official approval of the two bodies fostering its organization, as well as that of the Advisory Board for Medical Specialties and the Council on Medical Education and Hospitals of the American Medical Association.

The purpose of the Board will be the certification of specialists in the field of internal medicine, and the establishment of qualifications with the required examination procedure for such certification.

While the Board is at present chiefly concerned with the qualification and procedure for certification in the general field of internal medicine, it is intended to inaugurate immediately after July 1, 1937, similar qualification and procedure for additional certification in certain of the more restricted and specialized branches of internal medicine, as gastroenterology, cardiology, metabolic diseases, tuberculosis, allergic diseases, et cetera. Such special certification will be considered only for candidates who have passed at least the written examination required for certification in general internal medicine. The operation of such a plan will require the active participation and cooperation of recognized representatives from each of such special fields of medicine.

The first written examination will be held in December, 1936, and candidates successful in this written test will be eligible for the first practical or clinical examination which will be conducted by members of the Board near the time for the annual session of the American College of Physicians at St. Louis in April, 1937. The second practical examination will be held at Philadelphia near the time of the annual session of the American Medical Association in Atlantic City in June, 1937.

Application blanks and further information can be obtained by addressing the office of the chairman, Walter L. Bierring, M.D., 406 Sixth Avenue, Des Moines, Iowa, U. S. A.

Books Received

CONTRACEPTION AS A THERAPEUTIC MEASURE. By Bessie L. Moses, M.D. 90 pages. The Williams & Wilkins Company, Baltimore, 1936.

MEDICAL HISTORY OF CONTRACEPTION. By Norman E. Hines, Ph.D. Illustrated, 521 pages. The Williams & Wilkins Company, Baltimore, 1936.

A MANUAL OF PRACTICAL OBSTETRICS. By O'Donel Brown, assistant gynecologist, Sir Patrick Dun's Hospital, Dublin, etc. With 10 plates, some in color, and 236 illustrations, 363 pages. William Woods & Company, Baltimore, 1936.

SYPHILIS AND ITS TREATMENT. By William A. Hinton, M.D., Boston, Mass. 321 pages. The Macmillan Company, New York, 1936.

GYNECOLOGY FOR NURSES. By Harry Sturgeon Crossen, Professor Emeritus of Clinical Gynecology, Washington University School of Medicine, etc., and Robert James Crossen, Instructor in Clinical Gynecology and Obstetrics, Washington University School of Medicine, etc. Second edition, with 356 engravings including one color plate. 316 pages. The C. V. Mosby Company, St. Louis, 1936.

POST-GRADUATE SURGERY. Edited by Rodney Maingot, Senior Surgeon to the Royal Waterloo Hospital and to the Southend General Hospital, etc. Volume II. With 1134 figures in the text. 3572 pages. D. Appleton-Century Company, New York, 1936.

THE PATIENT AND THE WEATHER. By William F. Peterson, M.D. Volume I, Part 2. Autonomic Integration. Illustrated, 781 pages. Edwards Brothers, Inc., Ann Arbor, Mich., 1936.